Eyelid Radiotherapy-Treated Basal and Squamous Cell Carcinomas: A Case Series

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ABSTRACT

Introduction: This case report aims to showcase the successful application of electron hypofractionated radiotherapy in the treatment of eyelid basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).

Cases Presentation: Two cases are presented involving a 91-year-old Greek female with nodular BCC and an 88-year-old Greek male with ulcerative SCC. Both cases were treated with electron 10MeV irradiation using an ELEKTA 5-15MV linear accelerator. In the first case, a patient with advanced dementia presented with left-upper-eyelid nodular BCC. Following confirmation through biopsy and imaging, hypofractionated electron-beam radiotherapy was chosen, leading to gradual recession of the lesion and no recurrence at the one-year follow-up. In the second case, an elderly male with comorbidities had right-upper-eyelid ulcerative SCC. After systemic evaluation ruled out metastasis, the patient underwent hypofractionated radiotherapy, resulting in unexpected lesion shrinkage, resolution, and absence of recurrence at the 6-month and one-year follow-ups.

Conclusions: Hypofractionated electron-beam radiotherapy emerges as an effective and well-tolerated alternative for eyelid tumors, particularly in cases where surgical excision is challenging or contraindicated.

KEYWORDS

basal cell carcinoma; squamous cell carcinoma; electron hypofractionated radiotherapy; reverse koebner

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INTRODUCTION

Basal cell (BCC) and squamous cell carcinomas (SCC) are the two most common malignant neoplasms of the eyelids (1–3). Both BCC and SCC primarily involve the lower lid margin and inner canthus (4, 5). Although BCC is a low metastatic tumor, it is locally destructive and invasive to deeper structures, but rarely intraocularly. If BCC is left untreated, it may result in serious aesthetic and functional implications due to orbital invasion (6). On the other hand, SCC tends to metastasize more often than BCC, with lymph node and distant metastases threatening patients' life (7, 8). It is very important to distinguish them from other eyelid lesions and incisional biopsy is mandatory when there is suspicion of such lesion. If the diagnosis of SCC is confirmed, the patient should be checked extensively for systemic involvement. A series of treatment options have been described for BCC and SCC. The non-surgical options include cryotherapy, radiation, topical 5-fluorouracil, topical imiquimod, and photodynamic therapy. Additionally, systemic therapies have emerged for advanced cases, such as Erivedge (Vismodegibum), a hedgehog pathway inhibitor approved for the treatment of locally advanced or metastatic BCC (9), and Libtayo (Cemiplimabum), a PD-1 inhibitor used in advanced cutaneous SCC (10). These targeted therapies offer alternative treatment options for patients unsuitable for surgery or radiation. However, for both malignancies, surgical excision remains the gold standard therapeutic intervention (11). The treatment of choice depends on the physician's preference and the patient's characteristics.

Radiotherapy (RT) has been established as a viable treatment modality for BCC and SCC, particularly in the periocular area. RT offers several advantages, such as the preservation of anatomical structures and function, making it an appealing option for cases where surgical intervention may pose challenges. Additionally, RT is non-invasive, making it suitable for elderly patients or those with significant comorbidities who may not be ideal candidates for surgery (12, 13).

Despite its advantages, RT for BCC and SCC of the periocular area has its limitations. One of the primary concerns is the potential damage to surrounding healthy tissues, which may lead to adverse effects. Furthermore, the efficacy of RT can be influenced by factors such as tumor size, location, and histological characteristics. Thus, careful consideration and individualized treatment planning are crucial to optimize outcomes and minimize potential complications (14).

The application of hypofractionated radiotherapy has demonstrated effectiveness and excellent tolerability, yielding favorable cosmetic results (15). Additionally, the radiotherapy regimen offers convenience to patients by minimizing the required visits to Radiotherapy centres.

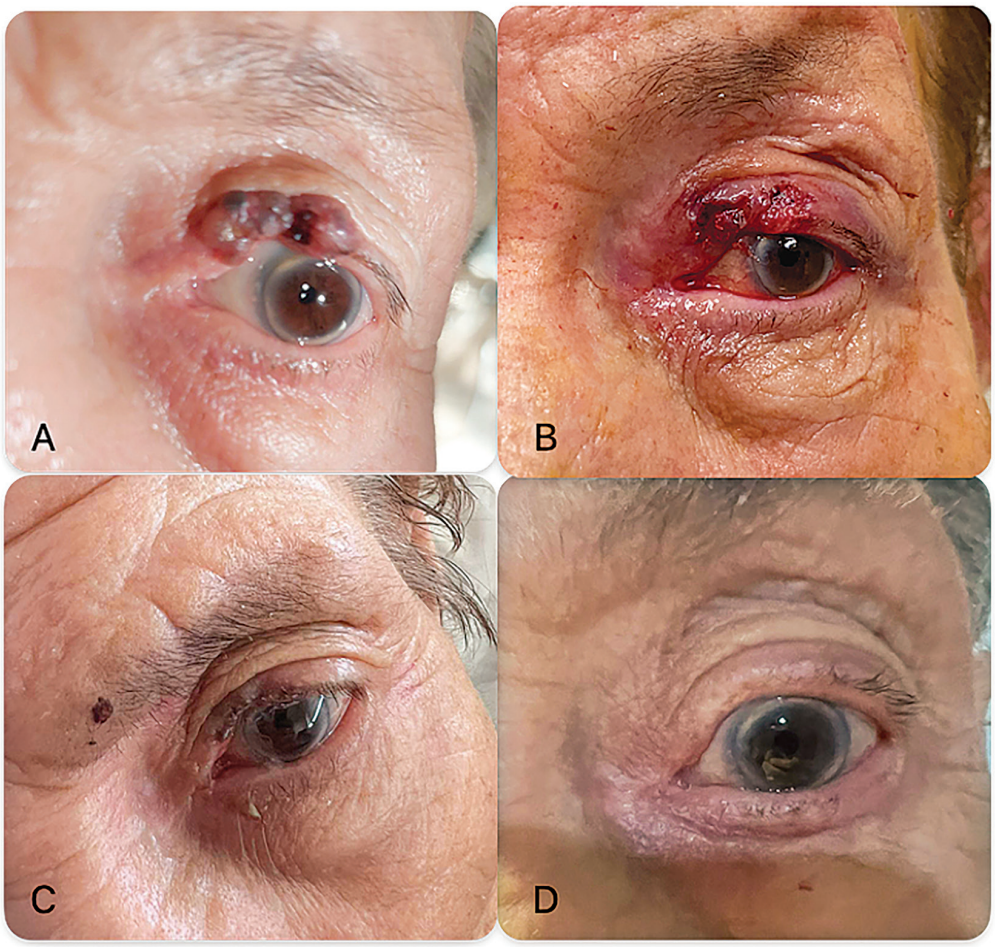

Fig. 1 Basal Cell Carcinoma of the left upper eyelid. A. Preoperative clinical appearance, B. Clinical picture immediately after biopsy, C. 1 week post hypofractionated electron-beam radiotherapy, D. 1-year-follow-up after hypofractionated electron-beam radiotherapy.

Within this context, we present two cases of BCC and SCC, both treated successfully with electron hypofractionated radiotherapy.

CASE PRESENTATION

FIRST CASE

A 91-year-old Greek female was referred to our oculoplastic department in December 2022 for a left-upper-eyelid nodular and ulcerative lesion with well-defined borders, loss of eyelashes, and small telangiectatic vessels on its surface (shown in Fig. 1A). The patient had advanced dementia and no other significant medical history. She was bilaterally pseudophakic with no other ocular pathology. A biopsy was performed and confirmed the presence of nodular BCC (shown in Fig. 1B). Orbit Magnetic resonance imaging (MRI) excluded metastasis to the orbit and neighbouring tissues. Taking into account the age of the patient, the location, and the extent of the lesion, treatment options were discussed with the patient, who opted to undergo radiotherapy. She was then referred for treatment and underwent hypofractionated electron-beam radiotherapy as the best treatment option for her, recommended by the radiotherapist. She was reviewed one week (shown in Fig. 1C) and three months after radiation therapy and showed gradual recession of the lesion. At the one-year follow-up, the patient had no signs of tumor recurrence on clinical examination (shown in Fig. 1D).

SECOND CASE

An 88-year-old Greek male was referred to our oculoplastic department in September 2022 for a right-upper-eyelid large ulcerative lesion (shown in Fig. 2A). Physical examination and slit-lamp biomicroscopy revealed a flat, ulcerative, fleshy, hemorrhagic lesion of about 3 cm in diameter, with irregular borders and scattered necrotic areas. His medical history included cardiac failure, asthma, diabetes mellitus type II, hyperuricemia, and normocytic anemia (with hemoglobin equal to 8.6 g/dL). His ocular history was unremarkable. Histopathological examination of a skin biopsy specimen taken one week later from the lesion showed features consistent with SCC. Therefore, he was first referred to a dermatologist, who suggested head, neck, chest, and abdominal Computed tomography (CT) to stage the tumor and exclude other malignancies. Orbit CT and MRI revealed a 2.7 cm cross-diameter heterogeneously enhanced soft-tissue mass in the right upper eyelid inner canthal area with intact eye globe, free retrobulbar spaces, as well as normal and symmetric imaging of the extraocular muscles and optic nerves bilaterally. A lymph node of 15 mm in diameter was detected in the left supraclavicular region and lymph nodes of marginal diameter were detected in the left axillary area. A non-clearly defined, hypo-enhancing, large liver mass was also detected. The detected lymph nodes and the liver mass were evaluated by radiotherapists and oncologists and were considered random, irrelevant to the skin carcinoma, based on the CT and MRI imaging findings and the radiologists' suggestions. As a result, the full systemic examination turned negative and hypofractionated electron-beam radiotherapy was selected as the most appropriate therapy, taking into consideration the patient's age as well as the extent and the location of the lesion. At the 2-week follow-up after biopsy, the lesion was unexpectedly significantly shrunk (reduction of about 1 cm) (shown in Fig. 2B), which was attributed to possible reverse Koebner phenomenon.

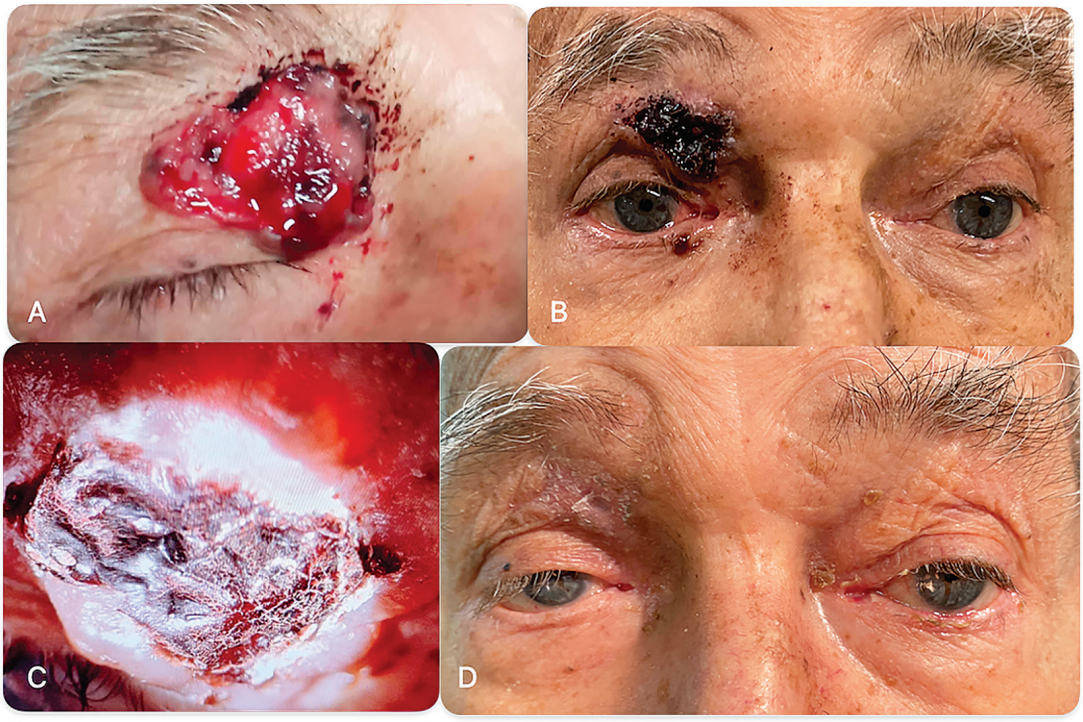

Fig. 2 Squamous Cell Carcinoma of the right upper eyelid. A. First examination in our oculoplastic department, B. two weeks after biopsy, C. one week after radiotherapy, D. four weeks after completing the irradiation cycle.

One week following radiotherapy, the lesion was further reduced in size to approximately 1.5 cm (shown in Fig. 2C). Four weeks after completing the irradiation cycle, an almost complete resolution of the tumor was observed with clinical appearance of scar tissue present (shown in Fig. 2D). A post-radiotherapy biopsy was performed at the 6-month follow-up, which revealed no presence of cancer cells. At the one-year follow-up, the patient had no signs of tumor recurrence on clinical examination.

Both patients were treated with electron 10MeV irradiation, using an ELEKTA 6-15MV linear accelerator. The choice of 10MeV energy was based on the fact that a lower, e.g. 6MeV, beam energy is associated with a 20% reduction of the surface radiation dose, which would demand a 1,5 cm bolus material over the lesion to assure 100% of the dose to the cancer surface. This would allow an adequate dose coverage up to a depth of no more than 1 cm (https://oncologymedicalphysics.com/electron-therapy-physics/). A beam of 10MeV energy on the lesion surface covered by 1–1.5 cm bolus material brings 100% of the radiation dose to the lesion's surface, allowing 90% of the dose to cover a depth of around 1–2 cm to assure inclusion of possible subclinical deep tumor invasion in the high dose area. Thus, a 1–1.5 cm thick bolus material was applied over the lesion before irradiation. A standard electron beam applicator of 6 × 6 cm was used, and lead blocks were applied on the applicator tray to shape the radiation field as demanded. An appropriate angle of the beam direction was considered by rotating the LINAC gantry and/or table to avoid critical structures like the eyeball and lens. The patient was instructed to look at a fixed point to facilitate the maximum possible distancing of the eye lens. According to the underlying tissue/organ, an individualized margin of 0,2–1 cm around the lesion defined the PTV. Narrower margins, for example, were necessary at the areas where the tumor of the eyelid borders the eyeball. The total dose delivered was 36 Gy, with 6 Gy fractions and three fractions per week, within 12 days. There were no adverse events during or after irradiation in either reported case. Mild erythema of no clinical significance was observed, and none of the patients had developed fibrosis, shrinkage, or other complications at the last follow-up.

DISCUSSION

Eyelid skin malignancies, including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), are among the most frequently encountered tumors in ophthalmic practice (3). They present significant management challenges due to their location and their potential for functional and cosmetic consequences (16). This series presents two cases of eyelid BCC and SCC, treated with electron 10 MeV irradiation, emphasizing the importance of a multidisciplinary approach involving ophthalmologists, dermatologists, pathologists, radiotherapists, and oncologists to ensure optimal patient outcomes, especially when the clinical picture shows advanced signs of the disease.

Both cases presented malignancies in the upper eyelid. It is known that both BCC and SCC mainly involve the lower lid margin and inner canthus. When a skin lesion appears in the upper eyelid and outer canthus, the diagnosis of SCC is more common than the diagnosis of BCC (3). In both cases, the diagnosis was confirmed with a biopsy. Interestingly, a significant reversal of the skin lesion was observed in the second case between the biopsy and the first 20-day follow-up. This is compatible with reverse Koebner response, which is the nonappearance or disappearance of the lesions of particular dermatoses at the site of injury (17). The exact etiopathogenesis of reverse Koebner phenomenon is poorly understood. A few previous reports of reverse Koebner phenomenon are available in the literature for several skin lesions, such as psoriasis, vasculitis, and primary cutaneous follicle center lymphoma following skin biopsy (17–19), however, there is no previous report of reverse Koebner phenomenon in eyelid SCC.

Taking into account the tumors' characteristics, the age and comorbidities of the patient, the patients' preference, as well as the recommendation by the radiotherapist, it was decided to perform electron 10 MeV irradiation in both patients, instead of surgical excision. Kilovoltage or electron beam radiotherapy has been routinely used for the treatment of superficially located tumors, including squamous cell and basal-cell carcinomas (20, 21). Although the first-line therapy of BCC and SCC remains the surgical excision, hypofractionated radiotherapy, as herein applied, has been proved effective and well tolerated, with good cosmetic outcomes (22). Moreover, the radiotherapy schedule is convenient for patients as it reduces the number of visits to the Radiotherapy centers and alleviates the waiting lists in busy departments. The biological dose equivalent to 2Gy (EQD2) for the 6×6Gy schedule is 60Gy, calculated for an α/β-ratio of 4Gy for normal tissue late toxicity (23). Although the EQD2 for a tumor α/β-ratio equal to 10Gy is lower (48Gy), the biological dose is increased due to the acceleration of the overall treatment time by 4 weeks compared to a conventionally fractionated radiotherapy scheme. Assuming a λ-value of 0.5Gy/day for skin cancer, the EQD2 with time correction (EQD2-T) becomes 62Gy.

Skin cancer of the eyelid and periorbital area, whether of squamous or basal-cell histology, is often localized. Although metastasis is infrequent, this mainly involves the preauricular or upper neck lymph nodes. Distant metastasis can evolve in a minority of patients, especially with squamous cell histology, large tumors, and extensive invasion of adjacent anatomical structures (24). Invasion to mediastinal and axillary lymph nodes should be considered exceptional, and the presence of small lymph nodes in these areas should be considered a random, still frequent event in elderly patients, irrelevant to the skin carcinoma. BCC has an extremely low rate of metastasis (0.03%), and the most common sites are the regional lymph nodes and the orbitofacial area (25). On the other hand, SCC tends to metastasize more often than BCC, primarily with preauricular and submandibular lymph node metastases at a rate of 3–6%, and with distant metastases located primarily at the lungs and the parotid gland at a rate of 1% (7, 8, 26).

Radiotherapy, with its ability to precisely target cancerous cells while minimizing damage to surrounding healthy tissue, has proven to be particularly advantageous

in cases where surgery may be challenging due to anatomical considerations or patient preferences. Several studies and clinical experiences have highlighted the successful outcomes of RT in achieving high cure rates for patients with early-stage periocular skin cancer. The effectiveness of RT in achieving local control and minimizing recurrence has established its role as a primary treatment modality for these cases. Additionally, RT has been instrumental in addressing locally advanced tumors, where surgical resection might pose challenges or compromise functional and cosmetic outcomes (20–22).

Although several studies are available in the relevant literature evaluating kilovoltage radiotherapy in eyelid tumors, to our knowledge, this was the first case report presenting cases of BCC and SCC treated with hypofractionated 10MeV electron-beam radiotherapy. Moreover, hypofractionated radiotherapy has been reported as a treatment for skin BCC and SCC (27, 28), however, no previous reports are available for the treatment of eyelid BCC and SCC with hypofractionated radiotherapy. Moreover, although few reports of reverse Koebner phenomenon are available in the literature for several skin lesions, to our knowledge, there is no previous report of reverse Koebner phenomenon in eyelid SCC.

In conclusion, hypofractionated electron-beam radiotherapy seems to be an efficient treatment for patients with eyelid tumors when surgery is absolutely or relatively contraindicated. Moreover, a multidisciplinary approach involving ophthalmologists, dermatologists, pathologists, radiotherapists, and oncologists is suggested to ensure optimal patient outcomes.

STATEMENT OF ETHICS

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patients for publication of this case report and any accompanying images.

FINANCIAL DISCLOSURE

No financial support was received for this case report. None of the authors has any proprietary interests or conflicts of interest related to this submission. It is not simultaneously being considered for publication at any other journal.

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