Case Report

Adjuvant Mitomycin C with an Alternative Cycle Strategy after surgical Excision in Conjunctival Melanoma: A Case Report

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ABSTRACT

Melanoma of conjunctiva is a rare but aggressive malignancy that has a high probability of recurrence. Topical Mitomycin C (MMC) is being used more commonly as an adjuvant. Our report presents a female patient with a temporal, bulbar conjunctival pigmented mass. Malignant melanoma was confirmed by excision with amniotic membrane transplantation and adjunctive cryotherapy. Although there was initial recovery, recurrence occurred within three months. Adjuvant MMC 0.04% was started in four intermittent cycles, and each cycle was four days with a weekly pause. The regimen was also tolerated, and only mild ocular irritation was present. Six months follow-up showed that the lesion was partially regressed with visual acuity remaining normal. The present case demonstrates that adjuvant MMC using another cycle regimen is a possible and effective alternative to recurrent conjunctival melanoma.

Keywords: Conjunctiva, Melanoma, Conjunctival Neoplasms, Mitomycin C, Adjuvant therapy, Case report.

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INTRODUCTION

Conjunctival melanoma (CoM) is a rare eye cancer that recurs and is difficult to treat.[1] Recent international studies have shown that recurrence is a significant problem, with one in five patients at 5 years and over one-third at 10 years.[2] It poses a high risk of occurrence in patients who have advanced tumour stages. These results highlight the importance of effective adjuvant strategies which do not only lower recurrence but also help in retaining visual functions.[3]

Topical Mitomycin C (MMC) is an adjuvant therapy, especially in cases where there has been a poor excision margin or where radiation is unfeasible. Alternative methods of MMC cycle are becoming a topic of interest as a method to maximize the therapeutic effect of MMC and reduce its toxicity to the ocular surface.[4] Traditional continuous regimens can lead to keratoconjunctivitis, limbal stem cell depletion and delayed healing of the epithelia and thus the necessity to have individual dosing regimens. Recent literature has reported positive outcomes of neoadjuvant and adjuvant MMC with a different cycle regimen in patients with conjunctival melanoma, illustrating its clinical rationale, treatment response, and possible application in the optimization of treatment regimens in the rare, yet, formidable, malignancy.[5]

Case Presentation

A 75-year-old woman with a history of a dark mass on her left eye, which had continued to grow over the last

month, came to our tertiary hospital in January 2023. The lesion appeared as a small spot, nearly a pimple, and gradually increased in size. There was no pain, no blood loss, no discharge and she had no relevant past medical or family history. There was no history of eye trauma or surgery.

Her visual acuity was 5/15 in the right eye and 5/6 in the left. Slit-lamp examination revealed a well-defined, firm, pigmented mass on the temporal bulbar conjunctiva measuring approximately 1.0 × 1.0 × 0.5cm. The surface was firm, non-tender and without bleeding. A few feeder vessels were noted, along with some surrounding conjunctival pigmentation. The cornea and anterior chamber were clear. Intraocular pressure was within normal limits, and there was no lymph node enlargement on general examination (Figure 1).

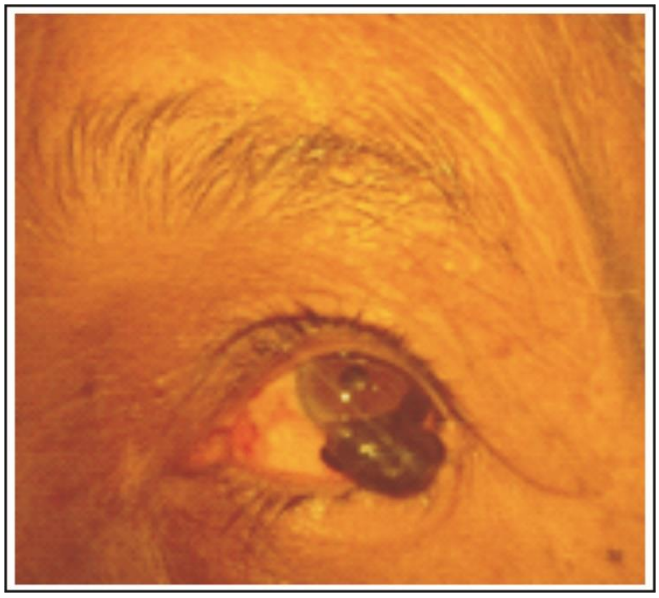

Figure 1: Clinical photograph of the left eye showing a well-demarcated, pigmented conjunctival mass located in the temporal region, measuring approximately 1.0 × 1.0 × 0.5 cm.

In June 2023, the patient underwent wide local excision of the lesion with adjunctive procedures including alcohol keratoconjunctival base removal (AKE), cryotherapy, and amniotic membrane transplantation (AMT) under general anaesthesia. Postoperatively, the ocular surface healed well with minimal discomfort, and no immediate complications were observed. Visual acuity remained stable, and the patient was managed with topical antibiotics, lubricants, and oral analgesics. At one-week and one-month follow-up visits, the surgical site appeared stable, although mild conjunctival hyperaemia persisted. Histopathological evaluation of the excised conjunctival tissue showed intact overlying conjunctival epithelium without evidence of tumour invasion. These features were consistent with the diagnosis of conjunctival melanoma (Figure 2).

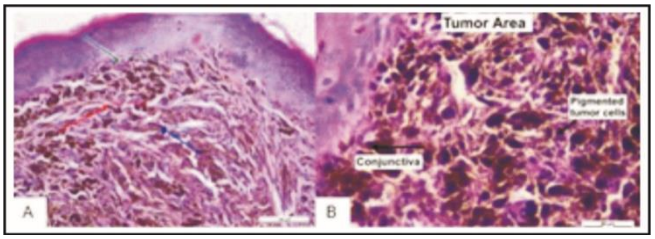

Figure 2: (A): Histopathological section of excised conjunctival tissue (H&E stain, 100 µm scale). Histopathological section of excised conjunctival tissue (H&E stain, 100 µm scale) showing nests and sheets of atypical melanocytic cells within the substantia propria. Arrows highlight (red) pigmented melanoma cells, (blue) nuclear atypia, and (green) intact conjunctival epithelium. **(B):** Histopathological section H&E stain, 400 µm scale). Tumour cells exhibited hyperchromatic, pleomorphic nuclei with abundant cytoplasm and coarse melanin pigment granules. The overlying conjunctival epithelium was preserved.

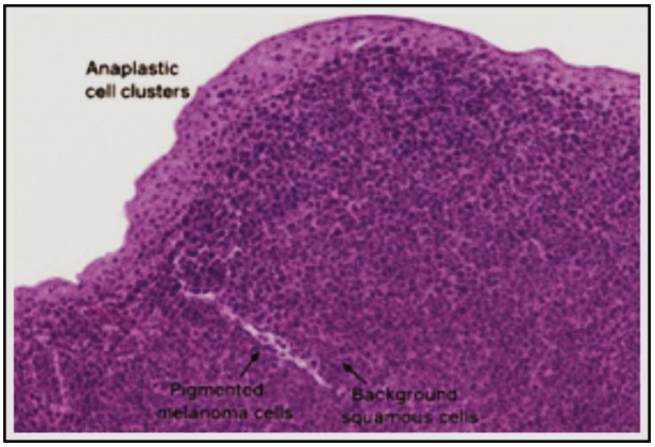

Figure 3: Impression cytology of the left bulbar conjunctival lesion showing a specimen measuring approximately 1 cm with ill-defined margins, prepared into two smears. Microscopic examination revealed clusters of anaplastic cells with round-to-oval nuclei, marked pleomorphism, hyperchromasia, and moderate cytoplasmic volume. Several cells contained dark brown pigmentation. The background demonstrated scattered squamous cells. These cytological features were consistent with recurrent malignant melanoma of the conjunctiva.

Despite initial improvement, impression cytology and fine needle aspiration biopsy performed in September 2023 revealed recurrent conjunctival melanoma (Figure 3). In view of the recurrence, adjuvant topical chemotherapy with Mitomycin C (MMC) was initiated. The treatment protocol consisted

of MMC 0.04% eye drops administered four times daily for four consecutive days per cycle, repeated over four cycles with a one-week drug-free interval between each cycle. The patient tolerated the regimen well, experiencing only mild side effects such as ocular irritation, redness, itching, and a foreign-body sensation. These adverse effects were managed with supportive therapy including preservative-free artificial tears and cold compresses.

Subsequent impression cytology of the recurrent lesion showed clusters of anaplastic melanocytic cells with hyperchromatic, pleomorphic nuclei and intracytoplasmic melanin pigment, consistent with recurrent malignant melanoma (Figure 3). Systemic evaluation, including liver ultrasound and orbital imaging, showed no evidence of intraocular extension or distant metastasis.

Following recurrence, the patient was started on topical chemotherapy with MMC 0.04%. Supportive therapy with preservative-free artificial tears was given to minimize ocular surface irritation. During therapy, the patient reported transient ocular discomfort, itching, redness, and a foreign-body sensation, which resolved with conservative management.

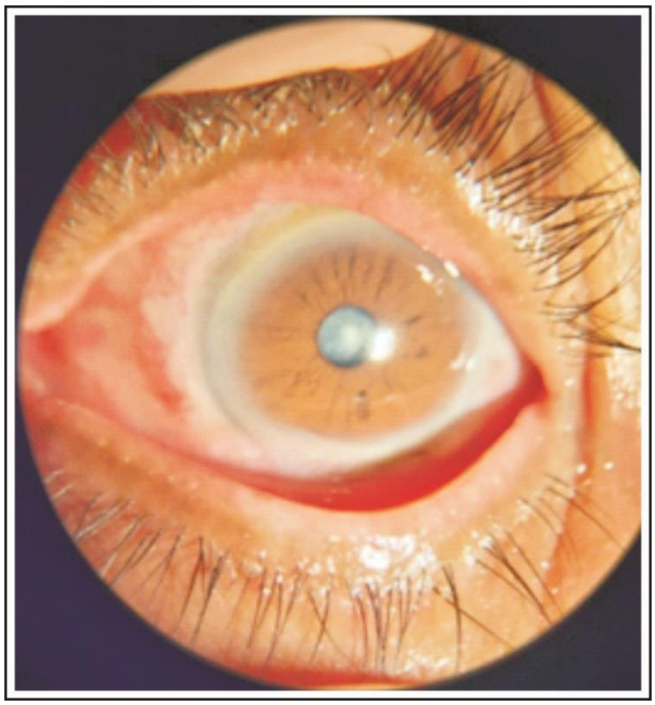

Figure 4: Slit-lamp image of the patient's left eye following four cycles of topical Mitomycin C 0.04%. The lesion shows decreased pigmentation and thickness compared to the initial presentation. The corneal surface remains clear without epithelial defects, stromal haze, or signs of limbal stem cell deficiency. Conjunctival hyperaemia is mild, reflecting good local tolerance to the therapy.

Serial follow-ups between October 2023 and February 2024 showed partial regression of the lesion with stable visual acuity (5/12 OD and 5/10 OS). Mild conjunctival symblepharon persisted, but no intraocular invasion or systemic metastasis was detected. At the most recent evaluation in February 2024, after four completed cycles of MMC, the patient reported no significant symptoms, and her ocular surface appeared stable (Figure 4). The patient continued monthly follow-up with topical lubrication and was scheduled for long-term monitoring to detect any future recurrence or progression.

DISCUSSION

MMC cross-links DNA, which inhibits replication and halts cells at the G1/S and G2/M phases.[6] It induces apoptosis in ocular melanocytic cells. This supports its use as an adjuvant in conjunctival melanoma, where some atypical cells may still be present after surgery. Topical MMC administered pre- or postoperatively in cyclic regimens can diminish recurrence, facilitating partial to complete lesion regression while minimizing ocular toxicity.[6,7]

Compared with the conventional continuous MMC regimens, often associated with recurrence rates approaching 25–30% and ocular toxicity in nearly one-third of patients, our intermittent cycle regimen demonstrated a sustained local response without severe surface complications. This outcome reinforces the growing evidence that strategic spacing of MMC cycles can preserve its cytotoxic potency while markedly improving ocular safety and patient comfort.[6,7]

Topical MMC has been shown to achieve regression of residual or recurrent conjunctival melanoma by inhibiting DNA synthesis and inducing apoptosis in dysplastic melanocytes. Our patient developed ocular irritation, redness, and swelling during MMC cycles, which required temporary treatment suspension, consistent with previously reported adverse event profiles.[6]

A major strength of this case is the detailed longitudinal follow-up and integration of both surgical and topical chemotherapeutic interventions, reflecting a multimodal approach that mirrors current best practices in ocular oncology. Furthermore, documentation of both histopathology and impression

cytology allowed precise monitoring of recurrence and treatment response. However, limitations include the single-patient design, which restricts generalizability, and the absence of advanced molecular profiling, which is increasingly relevant for prognostic stratification and targeted therapies.

The decision to postpone the initiation of topical Mitomycin C (MMC) until six months after excision was based on the need to ensure complete wound healing and ocular surface stability. MMC exerts its antitumor effect by inhibiting DNA synthesis and fibroblast proliferation, mechanisms that are also critical for normal tissue repair. If applied too early, while the conjunctiva and corneal epithelium are still regenerating, MMC can delay epithelial closure, impair stromal remodelling, and predispose the patient to complications such as persistent epithelial defects, limbal stem cell deficiency, conjunctival scarring, or even scleral thinning. By allowing sufficient time for re-epithelialization and restoration of the ocular surface barrier, the risk of long-term ocular morbidity is minimized while maintaining the therapeutic benefit of MMC in eradicating residual or recurrent melanocytic cells. This timing strategy aligns with recent recommendations emphasizing that adjuvant MMC should be introduced only after the surgical site has healed, thereby optimizing the balance between efficacy and safety.[8]

From a scientific perspective, the recurrence observed despite wide excision and cryotherapy is biologically plausible given the diffuse and multifocal growth pattern of conjunctival melanomas. The rationale for MMC use is supported by its capacity to address subclinical disease and residual atypical melanocytes that evade surgical margins. Nevertheless, long-term outcomes such as metastasis-free survival cannot be assessed from this case alone.

The case points out that frequent conjunctival melanoma should be monitored through close observation, and multimodal care using surgery and topical MMC can be used to gain local control. Clinicians, however, should be vigilant of both ocular surface toxicity and risk of recurrence, and customize treatment based on clinical response and tolerability.

In addition to the clinical and scientific factors, one must consider the personal experience of the disease and its treatment by the patient as this point of view would give significant information on how care would affect the quality of life. On the part of the patient, the first diagnosis and further recurrence was very traumatizing, especially when there was a fear of losing his sight. She said that she felt anxious when the tumour recurred following the surgery but relieved when the alternative of topical MMC was discussed in-depth. Even though she reported some discomfort during therapy including redness, irritation, and swelling, she said that the breaks provided by the treatment made it tolerable. She also told that the clinical team continuously followed up on her, and the effective communication with her helped her address the uncertainties of the disease. Nevertheless, she was grateful that she still has a working vision and could keep on with her everyday tasks, which is why medical intervention and psychological assistance during the care delivery process were incredibly valuable.

CONCLUSION

The case highlights the therapeutic benefits of topical MMC as adjuvant therapy in recurrent conjunctival melanoma especially where surgical therapy is not available or where complete excision of the tumour threatens recurrence. The patient tolerated MMC well, with only mild, manageable side effects, and showed no clinical progression of disease at six months post-treatment. While MMC is not without limitations most notably ocular surface toxicity and variable long-term efficacy it remains a valuable, minimally invasive adjunct in the multidisciplinary management of CoM. Given the rarity and aggressive nature of conjunctival melanoma, further prospective studies and long term follow up data are essential to establish standardized treatment protocols and to better define the role of MMC in improving patient outcomes.

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Conflict of Interest: Authors declared no conflict of interest.

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Evelyn Komaratih; Consultant Ophthalmologist: *Design, Literature Search, Manuscript Preparation.*