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# Long Term Outcome of Surgical Excision of Conjunctival Melanoma Combined with Mitomycin C Use: A Case Report

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## Abstract

**Purpose**: To report a case of conjunctival melanoma (CM) treated with excision and adjuvant mitomycin C.

**Methods**: This is a case report of a 51-year-old female with conjunctival melanotic lesion (10.5 × 5 mm), that was treated with complete surgical excision, combined with perioperative and intraoperative use of mitomycin C 0.02%. Lymphoscintigraphy with 0.3 mCi of technetium Tc-99m sulfur colloid and sentinel lymph node biopsy were also performed.

**Results:** Histological and immunohistochemical staining of the excised melanotic lesion [S-100 (+), Melan (+), Tyrosinase (+), HMB 45 (+)] confirmed the clinical diagnosis of Conjunctival Melanoma. Moreover, lymphoscintigraphy and sentinel lymph node biopsy were negative for tumor metastasis. Ten years postoperatively, there were neither signs of tumor recurrence or metastasis nor late postoperative complications due to mitomycin C.

**Conclusions:** Complete surgical excision combined with perioperative and intraoperative MMC 0.02% was safe and effective in preventing local recurrence in a case of conjunctival melanoma.

**Keywords:** Ocular surface; Conjunctiva; Neoplasia; Melanoma; Mitomycin C

## Introduction

Conjunctival melanoma (CM) is a rare malignant tumor that may arise de novo or in conjunction with nevus or primary acquired melanosis with atypia. Therapeutic approach is based on full surgical resection of the lesion. Additionally, cryotherapy and topical chemotherapy with mitomycin C (MMC), 5-fluorouracil or interferon can be applied to minimize the risk of recurrence [1].

Mitomycin-C is an antimetabolite/antibiotic which is mostly used systemically in cancer chemotherapy. MMC binds to DNA's double helix during any phase of cell cycle, inhibits DNA synthesis and function and therefore it does not permit the replication of cells.

We report a case of CM T1bN0M0 treated with complete surgical excision and adjuvant MMC 0.02% use.

## Case Report

In May 2005 a 51 year old Caucasian female, presented at the Cornea Service complaining of a congenital melanotic mass in her right eye that significantly increased in size during the last few months. Slit lamp examination revealed a melanotic cystic nodular lesion (10.5 × 5 mm), at the temporal part of the perilimbal, interpalpebral, bulbar conjunctiva equal to two quadrants (Figure 1). Preauricular and submandibular lymph nodes were not palpable.

Surgical procedure was scheduled and eye drops of MMC 0.02% q.i.d. for 2 weeks along with frequent use of non-preserved artificial tears were prescribed. During surgery performed in June 2005, after complete excision with around 2 mm safety margin, MMC 0.02% for 5 minutes was applied using sterile sponge, followed by copious irrigation with 30 ml saline. Histological and immunohistochemical staining of the melanotic lesion [S-100 (+), Melan (+), Tyrosinase (+), HMB 45 (+)] confirmed the clinical diagnosis of CM. Maximum penetration depth of the CM was 3 mm and the specimen margins were free of malignant cells (Figure 2).

After histological confirmation lymphoscintigraphy using subconjunctival 0.3 mCi of Technetium Tc-99m sulfur colloid, followed by sentinel lymph node (SLN) biopsy were performed [2]. Sentinel nodes were identified even though blue-dye, known to increase accuracy of scintigraphy, was not added to Technetium. First order SLNs were identified in the parotid (preauricular) region and second order in the submandibular area. Both lymph nodes were found free of malignancy in histological examination as well as in immunohistochemical staining with antibodies against S-100 and HMB 45. There were no intraoperative or postoperative complications. According to the 2010 American Joint Committee on Cancer clinical staging classification for CM was T1bN0M0, while pathological staging was pT1c pN0 cM0 and histologic grade due to previous presence of congenital nevus was G1.

Conjunctival epithelium covered the excision area within 5 days. Postoperatively, 3 two week courses of topical MMC 0.02% eye drops q.i.d, along with frequent use of artificial tears were prescribed at months 1, 3 and 6. Complete patient work-up was scheduled, including ultrasound, CT and MRI of the abdomen, head, neck and chest CT, as well as PET scan with FDG (F-18-fluprdeoxyglucose). All of the above were negative for tumor related metastasis. During follow-up, elective repetition of some of the above tests was performed as ordered by the general surgeon (ZO).

The patient completed 10 years of follow-up with no sign of local recurrence or tumor metastasis (Figure 3). No early or late complications due to MMC were observed.

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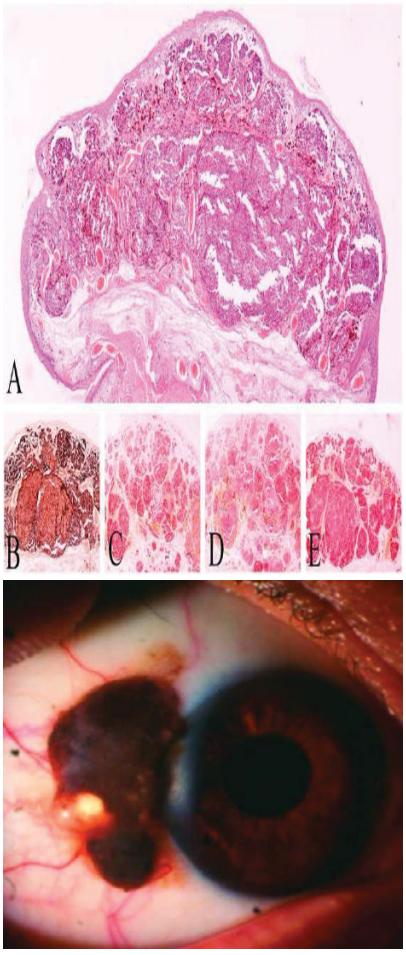


**Figure 1:** Right eye conjunctival melanoma at the interpalpebral, bulbar conjunctiva.

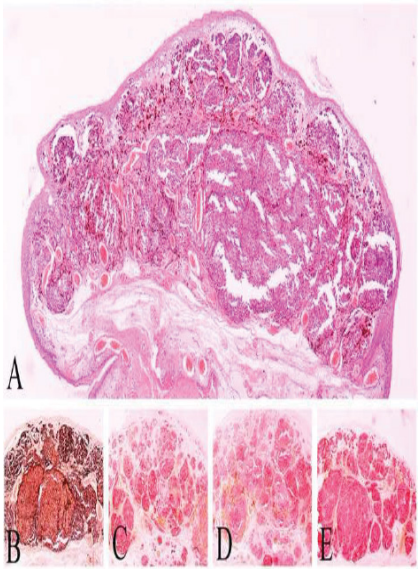


**Figure 2:** Magnification X40. (A) Panoramic view of CM with melanin production by tumor cells. Widespread invasion of the substantia propria and melanoma thickness is 3 mm. H&E stain. (B) Histochemical stain Masson Fontana evidences profuse melanin pigment production. Malignant melanocytes showed strong positivity (red color) in immunohistochemical stains Melan A (C), HMB-45 (D) and Tyrosinase (E).

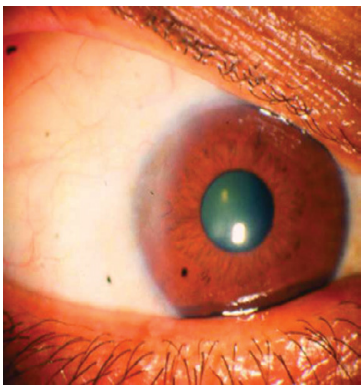

**Figure 3:** No recurrence 10 years after excision with adjuvant mitomycin C.

## Discussion

Conjunctival melanomas are malignant tumors of proliferating melanocytes from the neural crest. Differential diagnosis of CM mainly includes ocular or oculodermal melanocytosis, primary acquired melanosis and conjunctival nevi. MMC has been used in ophthalmology as an adjuvant treatment in a variety of ophthalmic conditions, such as other ocular surface neoplasia of the cornea and conjunctiva [2-5] as well as ocular pemphygoid, following trabeculectomy, pterygium and refractive surgery. In the largest published series of patients with PAM treated by topical Mitomycin C8 all patients had complete or partial response to treatment with no permanent side effects. In 11 out of 12 patients the pigmentation disappeared or significantly reduced while in only one of them had PAM re-growth and treated again by topical MMC successfully.

The exact concentration in the solution of MMC and the duration of application on the eye is still under examination in order to ensure its prophylactic action with minimal adverse effects.

The literature regarding the topical use of MMC for the treatment of CM is limited [3-9], due to the low incidence of the tumor (0.024 per 100.000 people). Most publications are case reports or small case series. Mitomycin-C can be used as primary treatment, as an adjuvant treatment to surgical excision or intraoperatively. The 0.02% or the 0.04% concentration of MMC is used, either as eye drops (3 cycles of 2 weeks, one drop four times per day) or intraoperatively (with a surgical sponge for three minutes). In the literature, we found only two cases of CM treated with intraoperative use of MMC 0.04% after surgical resection, with no recurrence 20 months postoperatively. Out of five patients with CM classified as T2N0M06, 8, three were treated with MMC 0.04% as adjuvant treatment to surgical resection (with no recurrence) and 2 as first line treatment (one of them with local recurrence combined with metastatic lesions). The selection of 0.02% MMC concentration in our case is based on our experience with its use in pterygia and ocular surface neoplasia [10-12] as being safe and effective. Damato et al suggest the 0.03% topical use as being more effective than 0.02% and safer than the reported 0.04% in most studies. The authors however mention that there is no consensus over the concentration of MMC and emphasize on the proper surgical excision and proper instrumentation handling to avoid iatrogenic tumour seeding [13].

We present a case of CM (pT1c pN0 cM0) treated with complete surgical excision and perioperative (eye drops) and intraoperative use of MMC 0.02% as a chemotherapeutic agent. The lesion showed several good prognostic features. Clinically, it was located at the temporal interpalpebral area, presenting as a unifocal mass without involvement

of the caruncle, plica semilunaris, eyelid margins or forniceal conjunctiva. However, histopathologically the maximum tumor thickness was 3 mm (more than 1.5 mm), but without orbital invasion. Ten yeas postoperatively, there were no signs of tumor recurrence or metastasis, and no early or late postoperative complications due to MMC. In this case, we also present the complete work-up for local metastasis including lymphoscintillography and lymph node biopsy, as well as full screening for distant metastasis.

In conclusion, complete surgical excision combined with perioperative and intraoperative MMC 0.02% was effective in preventing local recurrence of a pT1c grade conjunctival melanoma, 10 years post-operatively. Complete work-up for local as well as distant metastasis is recommended in such cases, since melanoma is known to be a devious type of malignancy.

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