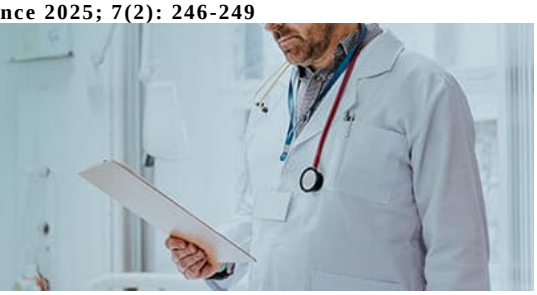
International Journal of Research in MEDICAL SCIENCE



ISSN Print: 2664-8733
ISSN Online: 2664-8741
Impact Factor (RJIF): 8.35
IJRMS 2025; 7(2): 246-249
www.medicalpaper.net
Received: 19-07-2025
Accepted: 22-08-2025

Zahrah Firdaus
[1] Department of Ophthalmology, Dr Soetomo General Academic Hospital, Surabaya, Indonesia
[2] Department of Ophthalmology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Susy Fatmariyanti
[1] Department of Ophthalmology, Dr Soetomo General Academic Hospital, Surabaya, Indonesia
[2] Department of Ophthalmology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Evelyn Komaratih
[1] Department of Ophthalmology, Dr Soetomo General Academic Hospital, Surabaya, Indonesia
[2] Department of Ophthalmology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Michelle Anisa Ujianto
[1] Department of Ophthalmology, Dr Soetomo General Academic Hospital, Surabaya, Indonesia
[2] Department of Ophthalmology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Chandra Prabaswara
[1] Department of Ophthalmology, Dr Soetomo General Academic Hospital, Surabaya, Indonesia
[2] Department of Ophthalmology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Corresponding Author:
Susy Fatmariyanti
[1] Department of Ophthalmology, Dr Soetomo General Academic Hospital, Surabaya, Indonesia
[2] Department of Ophthalmology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Mitomycin C as a Chemotherapeutic Adjunct in Conjunctival Malignant Melanoma: Clinical Outcomes from a Case Report

Zahrah Firdaus, Susy Fatmariyanti, Evelyn Komaratih, Michelle Anisa Ujianto and Chandra Prabaswara

DOI: https://www.doi.org/10.33545/26648733.2025.v7.i2d.159

Abstract
Conjunctival malignant melanoma is an uncommon but aggressive ocular surface cancer with a significant risk of recurrence and metastasis. Standard treatment comprises wide local excision with cryotherapy; nevertheless, incomplete excision frequently occurs, necessitating adjuvant therapy. Topical Mitomycin C has emerged as a useful adjuvant for killing residual tumor cells while protecting ocular tissues. We present the case of a 74-year-old male with a rapidly growing pigmented conjunctival lesion of the right eye, coupled with tears and mucous discharge. Ocular examination revealed a nodular, pigmented conjunctival mass (10 × 4 mm) with feeder vessels, stretching from 6 to 10 o'clock on the bulbar conjunctiva. Visual acuity was 3/60 in the right eye. The patient had broad local excision with cryotherapy and amniotic membrane transplantation. Histopathology confirmed conjunctival malignant melanoma with tumor cells at numerous margins, indicating incomplete excision. Adjuvant topical Mitomycin C 0.04% given 2.5 months after excision and provided in four cycles (four consecutive days per cycle, four times daily, with one-week intervals). The patient tolerated the regimen with just minor conjunctival hyperemia. At 6-month follow-up, the ocular surface was stable, visual acuity improved to 20/63 in the right eye, and neither local recurrence or systemic metastasis was observed. This case illustrates the importance of adjuvant topical Mitomycin C as an effective and well tolerated therapy for conjunctival malignant melanoma with positive surgical margins. In older patients with systemic comorbidities, Mitomycin C is a practical organ-preserving approach for local tumor treatment. Long term surveillance remains crucial to detect late recurrence or metastasis.

Keywords: Conjunctival malignant melanoma; Mitomycin C; Adjuvant chemotherapy; Ocular surface tumor; Wide local excision

Introduction
Conjunctival malignant melanoma (CoM) is a rare yet aggressive ocular surface malignancy, constituting less than 1% of all melanomas. Recent multicenter data indicate local recurrence rates of approximately 19.1%, with the risk of recurrence increasing progressively over time to 36.9% at 10 years, particularly in eyes lacking adjuvant therapy (8.5% with adjuvant therapy) [1]. Additionally, systemic metastasis impacts approximately 22.3% of patients within a decade, with an advanced AJCC T-category markedly elevating metastatic risk [2]. These results highlight the necessity of extensive multimodal management strategies to reduce both local recurrence and systemic dissemination.

Radiotherapy and interferon-α2b are two examples of adjuvant therapies that have been used. However, topical Mitomycin-C (MMC) has become more popular as a useful addition because it can get rid of microscopic residual disease while keeping the structures of the eye intact. While prospective data is still scarce, recent studies have identified advanced T-subcategories, older age, and prior conjunctival surgery as significant predictors of recurrence [3]. Newer reviews also show how tumor location, growth pattern, cell type, and lymphatic invasion can help predict local recurrence and metastasis [4]. We describe an elderly patient with conjunctival malignant melanoma who underwent wide local excision, cryotherapy, amniotic membrane transplantation, and multiple cycles of adjuvant topical

MMC, to demonstrate the therapeutic advantages and clinical implications of MMC in high-risk disease.

Case report

A 74-year-old male farmer was referred with a progressively enlarging pigmented lesion on the right eye conjunctiva, first noticed approximately 1.5 years earlier and enlarging more rapidly over the last 8 months. The patient reported watering and mucous discharge but denied ocular pain, photophobia, or acute vision loss. Past medical history was significant for controlled hypertension on amlodipine 5 mg daily, a remote ischemic stroke more than 10 years earlier with residual mild facial palsy, and suspected hepatic cirrhosis. He had no history of diabetes mellitus or chronic kidney disease. Ocular history included bilateral cataract extraction more than 20 years ago without complications. He was a lifelong farmer, with no history of trauma or smoking.

On initial presentation in February 2024, best-corrected visual acuity was 3/60 in the right eye and 5/20 in the left. Slit-lamp examination of the right eye revealed a darkly pigmented, nodular, elevated conjunctival mass measuring 10 × 4 mm, extending from 6 to 10 o'clock on the bulbar conjunctiva, mobile, with irregular surface and prominent feeder vessels. The cornea and anterior chamber were clear. The left eye showed pseudophakia and mild visual reduction. Palpable lymphadenopathy was present in the left submandibular region. Intraocular pressures were normal. Systemic evaluation, including chest X-ray, revealed paracardial infiltrates raising the possibility of pulmonary inflammation or metastasis, though no definitive systemic spread was established.

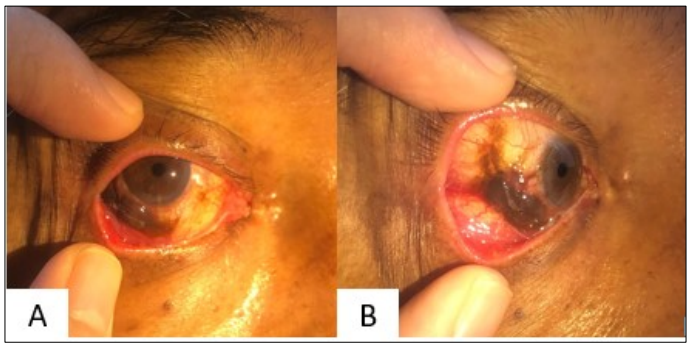


Fig 1: Slit-lamp image of the right eye at presentation.

(A) Slit-lamp image of the right eye at presentation (February 2024) showing a pigmented, nodular conjunctival mass (10 × 4 mm) extending from 6 to 10 o'clock with irregular surface and feeder vessels. (B) The lesion appears elevated with irregular pigmentation and prominent feeder vessels, consistent with conjunctival malignant melanoma, the cornea and anterior chamber were clear.

Courtesy of Dr. Soetomo General Hospital, Surabaya, Indonesia.

In February 2024, the patient came in with a pigmented conjunctival lesion in the right eye that had been getting bigger over time. The lesion had been present for over one year, with accelerated growth during the preceding eight months. In May 2024, the patient had a wide local excision of the conjunctival mass, along with cryotherapy and amniotic membrane transplantation. Histopathological examination confirmed malignant melanoma, with residual tumor cells identified at multiple surgical margins. After adequate ocular surface recovery, adjuvant topical Mitomycin-C (0.04%) was initiated in August 2024. The plan called for four treatment cycles, each lasting four days in a row, with a week between each cycle. The treatment was well tolerated, with only mild conjunctival hyperemia and tearing reported. At follow-up in October 2024, after completion of all cycles, the ocular surface remained stable, visual function had improved, and there was no evidence of local recurrence or systemic metastasis.

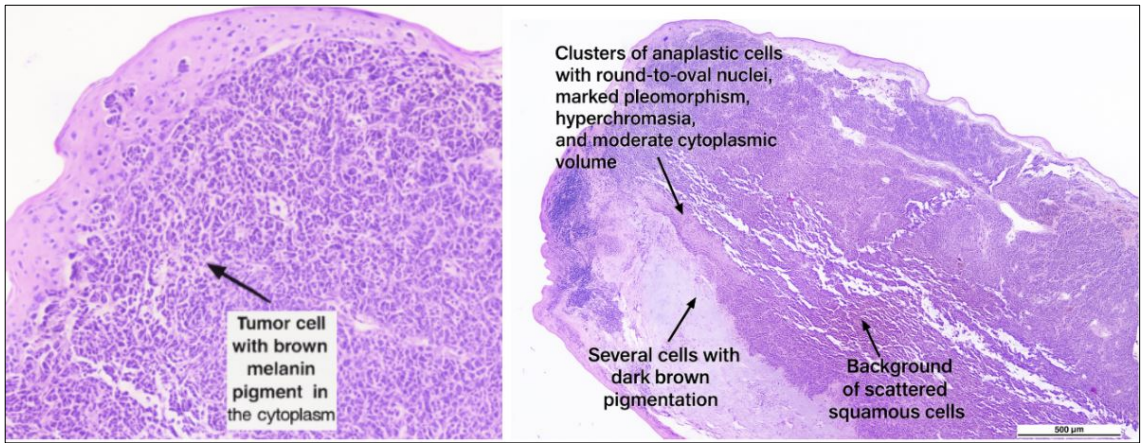


Fig 2: Histopathological section of conjunctival melanoma.

(Left Picture) Histopathological section of conjunctival tissue showing malignant melanoma. The image demonstrates nests and sheets of atypical melanocytic tumor cells with variable nuclear pleomorphism and prominent nucleoli. Some tumor cells contain coarse brown melanin pigment within the cytoplasm (arrow). The tumor cells infiltrate the conjunctival stroma, consistent with conjunctival malignant melanoma. Hematoxylin and eosin (H&E) stain, original magnification ×200. (Right Picture) Histopathological section of conjunctival melanoma

showing solid proliferation of anaplastic melanocytic cells with pleomorphic, hyperchromatic nuclei, prominent nucleoli, and cytoplasm containing brown pigment. Tumor cells are present at the superior, inferior, and basal margins, with a lateral clearance of 2 mm and a free medial margin of 10 mm.

Histopathological analysis of the removed conjunctival tissue indicated a solid growth pattern constituted of anaplastic melanocytic cells. The tumor cells had round-to-oval nuclei with strong pleomorphism, hyperchromasia, and large nucleoli, accompanied by copious cytoplasm, some of which contained dark melanin pigment. Paraffin-embedded slices taken on June 3, 2024, exhibited similar findings with areas of cystic atrophy and a high mitotic index (>20 mitoses per 10 HPF), indicating aggressive biological behavior.

Residual tumor cells were found at the superior (VC III/SVC III), inferior (VC IV/SVC IV), and basal (VC IV/SVC IV) margins, while the lateral resection margin exhibited a minimal clearance of 2 mm (VC II/SVC II). The medial resection margin exhibited a broader clearing of 10 mm (VC I/SVC I) and was devoid of tumor infiltration. These findings are consistent with malignant conjunctival melanoma, defined as invasive with close surgical margins and persistent disease at numerous boundaries.

From a clinical standpoint, the presence of remaining tumor cells at various margins and the high proliferative index imply a large risk of local recurrence and perhaps systemic metastasis. These findings underline the requirement of close postoperative surveillance and justify the use of adjuvant medicines, such as topical Mitomycin-C, to target persisting microscopic illness and reduce recurrence risk while preserving ocular function.

Surgical management consisting of extensive local excision with safety margins, intraoperative cryotherapy to surgical boundaries, and amniotic membrane transplantation to heal the ocular surface. Given the acceptable surgical margins, adjuvant topical MMC 0.04% was applied in four cycles. Each cycle contains four consecutive days of MMC instillation at four times daily, followed by one-week drug-free periods. Supportive therapy includes preservative-free artificial tears, topical antibiotics, and oral analgesics. The drug was tolerated with moderate ocular surface hyperemia and transient tears, without substantial keratopathy, limbal stem cell deficit, or systemic toxicity.

Serial follow-up indicated good ocular surface healing and increased right eye visual acuity to 20/63. No recurrence was found at the excision site during the 6-month observation period. Systemic assessment did not uncover evidence of metastatic illness. At the most recent checkup in October 2024, the conjunctiva remained stable, with mild chronic hyperemia controlled conservatively with lubricants. The patient continues to be evaluated for late recurrence or systemic spread.

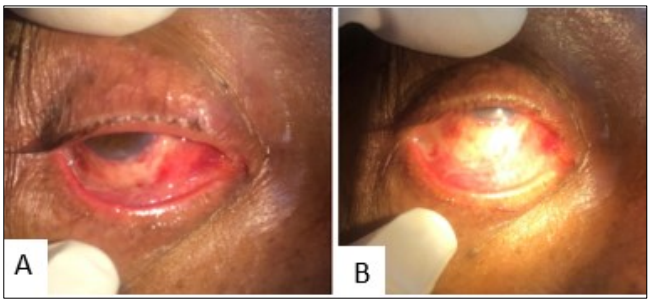


Fig 3: Postoperative follow-up of the right eye.

Postoperative appearance of the right eye following wide local excision of conjunctival malignant melanoma with adjunctive cryotherapy. (A) Early postoperative day showing conjunctival defect with well-apposed sutures at the superior margin. (B) The surgical site covered with amniotic membrane graft demonstrating good placement and adherence. The ocular surface shows satisfactory healing following wide local excision and adjuvant therapy. Best-corrected visual acuity improved to 20/63, with no evidence of recurrence at the excision site during the 6-month surveillance period (October 2024). Mild persistent conjunctival hyperemia was present but controlled with lubricants.

Discussion

Conjunctival malignant melanoma (CoM), albeit rare, offers considerable difficulties due to its tendency for local recurrence and systemic metastasis. A recent retrospective study from Japan reported local recurrence rates of 18.8% at five years and 31.5% at ten years, with metastasis in 32.4% of cases at ten years and a 5-year survival rate of 78.8% [6]. These findings underscore the necessity of long-term surveillance, particularly in patients with acceptable surgical margins.

Adjuvant treatment is necessary in high-risk scenarios. A comparative examination of topical Mitomycin-C (MMC) and interferon-α2b found that MMC achieved a considerably superior full remission rate (57% vs. 46%), with comparable recurrence rates of around 35%. Importantly, no metastases occurred in the MMC group, although 3.8% of interferon-treated patients experienced metastasis [8]. This supports the use of MMC as a successful adjunct to surgical excision.

The initiation of topical Mitomycin C (MMC) 2.5 months after excision of conjunctival melanoma is intended to balance effective adjuvant therapy with adequate wound healing. Immediate postoperative use of MMC can interfere with conjunctival repair, as it inhibits fibroblast proliferation and angiogenesis, both of which are essential for re-epithelialization and stromal remodeling. Allowing a healing interval of several weeks enables the surgical site to develop sufficient epithelial integrity, thereby reducing the risks of delayed closure, scleral thinning, or necrosis, while still addressing residual microscopic tumor cells that pose a risk of recurrence. Thus, delaying MMC until the conjunctiva has adequately healed provides a safer therapeutic window that maximizes antineoplastic efficacy while minimizing wound-related complications [8].

The role of neoadjuvant MMC has also been reported. A case report presented preoperative MMC 0.04% given for three weeks, which drastically reduced tumor size prior to excision with cryotherapy, followed by additional postoperative MMC cycles. This multimodal therapy achieved persistent local control with no recurrence after 32 months of follow-up [7]. Although limited, such findings demonstrate MMC may play a role both pre- and post-operatively in selected circumstances.

Beyond clinical results, molecular findings are increasingly altering prognostic evaluation. Mutations in BRAF, NRAS, TERT and NF1, coupled with chromosomal abnormalities such as 6p amplifications and 10q deletions, have been implicated in heightened metastatic potential [4, 5]. Such findings may in future drive tailored risk categorization and treatment decisions.

In this case, adjuvant topical MMC was chosen given good surgical margins and significant systemic comorbidities that prohibited radiation or systemic therapy. The medicine was well tolerated and efficient in obtaining short-term tumor control. However, vigilant long-term follow-up remains needed due to the potential for late recurrence and metastases.

The patient acknowledged satisfaction with the outcome, expressing joy that the pigmented lesion had been successfully eliminated and that vision improved in the affected eye. He recalled having some redness and tearing throughout Mitomycin-C therapy but saw these as manageable compared to the benefits of preserving his eye. He expressed gratitude for the continual monitoring and continuing follow-up, and affirmed trust in the chosen treatment strategy despite his varied medical difficulties.

Conclusion

Conjunctival malignant melanoma remains a rare but highly aggressive ocular surface malignancy with substantial risk of recurrence and metastasis. Surgical excision with adjuvant cryotherapy is the mainstay of treatment, yet positive surgical margins remain a challenge. This case demonstrates the potential benefit of adjuvant topical Mitomycin C (MMC) in achieving local tumor control when complete excision cannot be achieved. In our patient, multiple cycles of MMC 0.04% were well tolerated, with only mild conjunctival hyperemia and no severe ocular surface complications. At 6-month follow-up, the patient remained free of recurrence and systemic spread. This case highlights MMC as a practical, effective, and organ-preserving adjunct in the management of conjunctival melanoma, particularly in elderly patients with systemic comorbidities who may not tolerate alternative therapies such as radiotherapy or systemic chemotherapy. Long-term follow-up is critical, as late recurrence and metastasis are well documented.

Conjunctival malignant melanoma is an uncommon but extremely aggressive ocular surface tumor with great risk of recurrence and metastasis. Surgical excision with adjuvant cryotherapy is the basis of treatment, however good surgical margins remain a difficulty. This example highlights the possible usefulness of adjuvant topical Mitomycin C (MMC) in attaining local tumor control when total excision cannot be done. In our patient, numerous cycles of MMC 0.04% were well tolerated, with only minor conjunctival hyperemia and no serious ocular surface sequelae. At 6-month follow-up, the patient was clear of recurrence and systemic spread. This example highlights MMC as a practicable, effective, and organ-preserving adjuvant in the management of conjunctival melanoma, particularly in older patients with systemic comorbidities who may not tolerate alternative therapies such as radiotherapy or systemic chemotherapy. Long term follow up is crucial, as late recurrence and metastasis are well documented.

Acknowledgements

Funding

This study was not founded by any organization.

Patient's Consent

Researchers followed the guidelines set forth in the Declaration of Helsinki.

Conflict of Interest

Authors declared no conflict of interest.

Availability of Data and Materials

The data supporting the results of this case report are available from the corresponding author upon reasonable request.

References

1. Jain P, Finger PT, Fili M, Damato B, Coupland SE, Heimann H, *et al*. American Joint Committee on Cancer Ophthalmic Oncology Task Force. Conjunctival melanoma treatment outcomes in 288 patients: a multicentre international data-sharing study. Br J Ophthalmol. 2021;105(10):1358-64. doi:10.1136/bjophthalmol-2020-317646.
2. Jia S, Zhu T, Shi H, Zong C, Bao Y, Wen X, *et al*. American Joint Committee on Cancer tumor staging system predicts the outcome and metastasis pattern in conjunctival melanoma. Ophthalmology. 2022;129(7):771-80. doi:10.1016/j.ophtha.2022.01.012.
3. Vaidya S, Dalvin LA, Yaghy A, Pacheco R, Shields JA, Lally SE, *et al*. Conjunctival melanoma: risk factors for recurrent or new tumor in 540 patients at a single ocular oncology center. Eur J Ophthalmol. 2021;31(5):2675-85. doi:10.1177/1120672120946327.
4. Butt K, Hussain R, Coupland SE, Krishna Y. Conjunctival melanoma: a clinical review and update. Cancers (Basel). 2024;16(18):3121. doi:10.3390/cancers16183121.
5. Beigi YZ, Lanjanian H, Fayazi R, Salimi M, Hoseyni BH, Noroozizadeh MH, *et al*. Heterogeneity and molecular landscape of melanoma: Implications for targeted therapy. Mol Biomed. 2024;5(1):17. doi:10.1186/s43556-024-00183-1.
6. Tanabe M, Funatsu N, Akiyama M, Takaki KI, Fujii Y, Seki E, *et al*. Clinical features and prognosis of conjunctival melanoma in Japanese patients. Jpn J Ophthalmol. 2024;68(5):463-71. doi:10.1007/s10384-024-01064-0.
7. Mazzini C, Pieretti G, Vicini G, Nicolosi C, Virgili G, Giansanti F. Extensive conjunctival melanoma successfully treated with surgical resection and pre- and postoperative topical mitomycin C. Eur J Ophthalmol. 2021;31(6):NP71-4. doi:10.1177/1120672120947597.
8. Alvarado-Castillo B, Santa Cruz-Pavlovich FJ, Gonzalez-Castillo C, Vidal-Paredes IA, Garcia-Benavides L, Rosales-Gradilla ME, *et al*. Safety and efficacy of topical interferon alpha 2B and mitomycin C for localized conjunctival intraepithelial neoplasia: long-term report of their pharmacological safety and efficacy. BMC Ophthalmol. 2023;23(1):335. doi:10.1186/s12886-023-03141-1.

How to Cite This Article

Firdaus Z, Fatmariyanti S, Komaratih E, Ujianto MA, Prabaswara C. Mitomycin C as a Chemotherapeutic Adjunct in Conjunctival Malignant Melanoma: Clinical Outcomes from a Case Report. International Journal of Research in Medical Science 2025; 7(2): 246-249.