

## Resolution of Primary Acquired Melanosis with Atypia after Treatment with Topical Mitomycin C and Interferon Alfa-2b

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### Abstract

**Purpose:** To report a case of primary acquired melanosis (PAM) successfully treated with combined topical mitomycin C and interferon- $\alpha$ 2b.

**Case Report:** A 75-year-old man presented with an extensive unilateral pigmented lesion involving 360° of the bulbar conjunctiva, extending to the fornices and palpebral conjunctiva. Map biopsy confirmed PAM with local atypia. Treatment was initiated with mitomycin C 0.04% eye drops for two courses. Although the lesion markedly responded to the treatment, residual lesions justified further therapy. To avoid ocular surface toxicity induced by excessive mitomycin C exposure, interferon- $\alpha$ 2b eye drops were started and continued for 6 months. The pigmented lesion almost completely disappeared and no significant complication or recurrence was observed for 24 months.

**Conclusion:** Combination therapy using mitomycin C and interferon- $\alpha$ 2b for PAM with atypia may be recommended as an effective treatment modality, avoiding the ocular surface toxicity due to excessive mitomycin C exposure.

**Keywords:** Conjunctival Melanoma; Interferon- $\alpha$ 2b; Mitomycin C; Primary Acquired Melanosis

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### INTRODUCTION

Primary acquired melanosis (PAM) of the conjunctiva appears as a flat, brown pigmented lesion in the conjunctival epithelium. PAM with atypia is the most important precursor for conjunctival melanoma and its rate of progression to malignant melanoma has been reported up to 46%.<sup>[1]</sup>

The most commonly used treatments for PAM with atypia include surgical excision with cryotherapy and topical mitomycin C (MMC) or interferon- $\alpha$ 2b (IFN- $\alpha$ 2b).<sup>[2]</sup> MMC and IFN- $\alpha$ 2b are not only effective for treating conjunctival melanocytic tumors, but also have been used successfully for treatment of conjunctival squamous neoplasia, including conjunctival/corneal intraepithelial neoplasia (CIN) and squamous cell carcinoma (SCC).<sup>[2]</sup>

IFN- $\alpha$ 2b was used for patients with CIN or SCC

of conjunctiva in whom intolerance or recurrence of the tumor developed under treatment with MMC.<sup>[3-7]</sup> However, to the best of our knowledge, combined use of MMC and IFN- $\alpha$ 2b for treatment of conjunctival melanocytic tumors has not been reported yet.

### CASE REPORT

A 75-year-old man presented with extensive brown pigmented lesions of the conjunctiva in his left eye. On examination, visual acuity was 6/10 with pseudophakia in the right eye and 2/10 with 3+ nuclear sclerosis in the left eye. Fundus examination was unremarkable in both eyes. The lesion involved the whole bulbar and palpebral conjunctiva extending into the upper and lower fornices.

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Near the superotemporal limbus, a nodular portion of the lesion seemed to be encroaching onto the cornea. No further abnormal findings were seen on slit lamp examination in both eyes.

Map biopsy confirmed PAM with atypia especially in the nodular part of the lesion [Figure 1a-c]. Treatment was initiated with two courses of topical chemotherapy each lasting for 2 months composed of three cycles MMC 0.04% eye drops every 6 h. The first cycle lasted for 3 weeks followed by a 1-week gap to allow the ocular surface to recover, then the second cycle was initiated for 2 weeks followed by another 1-week treatment gap of MMC and finally, MMC was administered again for 1-week. After 1-month of rest, the second 2-month episode of treatment with MMC was implemented as described above. The lesion decreased in size and pigmentation in the middle of the second course of therapy [Figure 1d-f].

The second course of MMC therapy was interrupted in its final week because of severe discomfort of the patient. Thus, IFN- $\alpha$ 2b (1 million units/ml) eye drops were initiated every 6 h for 6 months, during which no significant topical or systemic side effect occurred [Figure 1d-f]. After 4 months, due to residual pigmentation close to the limbus and on the superior tarsal conjunctiva, the patient received INF- $\alpha$ 2b eye drops for more 3 months. No significant complications and no

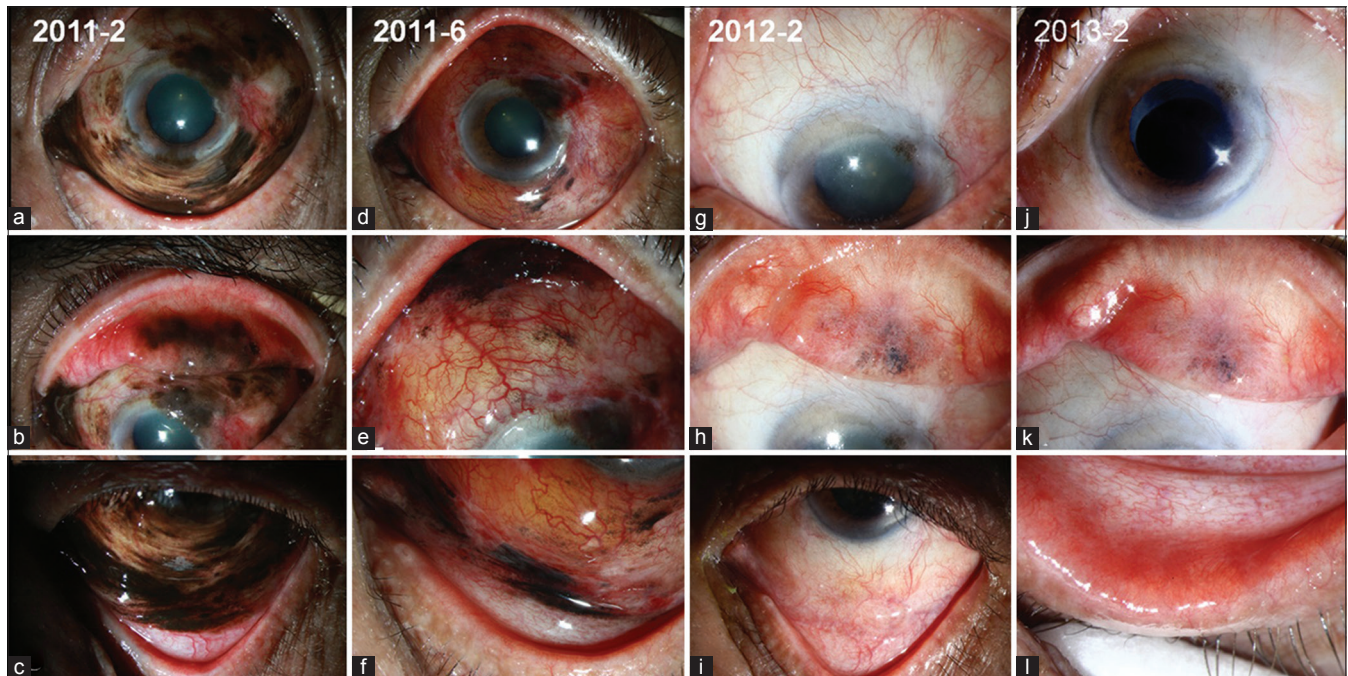
recurrence of the tumor were noted over 24 months follow-up [Figure 1g-l]. The cataract was operated at this point of time and visual acuity was 7/10 at final follow-up.

## DISCUSSION

Topical chemotherapy with MMC for conjunctival melanoma was introduced by Finger et al This approach offers potential benefits over surgery including less dependence on surgical margins, direct delivery of a high concentration of the chemotherapeutic agent to the tumoral tissue, treatment of tumor extension on the cornea and comfortable repetition.<sup>[8]</sup>

Finger et al used topical IFN- $\alpha$ 2b for PAM for the 1<sup>st</sup> time.<sup>[9]</sup> The agent incurs low toxicity to the ocular surface<sup>[10,11]</sup> and as compared to MMC, imposes a lower risk of complications such as corneal erosions, pain, conjunctivitis, punctal occlusion and scleral melting.<sup>[5]</sup> Over a mean follow-up period of 15-24.8 months<sup>[10,11]</sup> and 15 months,<sup>[10]</sup> complete clinical regression was reported in all treated patients except one subject with no systemic side effects.

Some investigators have used IFN- $\alpha$ 2b for patients with conjunctival CIN or SCC after intolerance to therapy or tumor recurrence following the application



**Figure 1.** Therapeutic trend of our patient with extensive primary acquired melanosis (PAM) in the left eye treated with topical mitomycin C (MMC) and interferon (INF)  $\alpha$ -2b; (a-c), appearance of the eye at presentation; Histologically confirmed PAM with atypia involved the bulbar and palpebral conjunctiva as well as the superotemporal cornea; (d-f), relative response to therapy in the middle of the treatment, note decreased size and pigmentation of the lesion; (g-i), Final result of treatment after receiving MMC followed by 6 months of therapy with INF- $\alpha$ 2b; (j-l), Appearance of the ocular surface after another year of follow-up, note more significant dilution of residual pigmentation without treatment.

of MMC.<sup>[3-7]</sup> Since MMC toxicity is dose-dependent,<sup>[3]</sup> replacing it with an effective topical medication with fewer side effects such as IFN- $\alpha$ 2b seems rational.

To our knowledge, the patient presented herein, is the first reported case of PAM successfully treated with topical MMC followed by long term topical IFN- $\alpha$ 2b. Further studies with larger sample size using such combined therapy as primary treatment for PAM and conjunctival melanoma are recommended.

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