

Corneal Displaced Conjunctival Melanoma: Rare Presentation of a Resilient Foe

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Abstract

A 49-year-old man with history of recurrent left conjunctival melanoma (CM) and primary acquired melanosis (PAM), which were treated over 13 years with excisional biopsies, cryotherapy, absolute alcohol, and two cycles of topical mitomycin C, presented with an elevated amelanotic corneal mass that was consistent with corneally displaced CM (CDCM). Therefore, he underwent wide excision of corneal and conjunctival base lesion, map biopsy and cryotherapy. In addition, he had lamellar sclerotomy to confirm clear margins, amniotic membrane transplantation, sentinel lymph node biopsy (SLNB) that failed to identify any pathologic nodes, and complete metastatic work-up. This case demonstrates that CM has a high risk of recurrence and these recurrences can be amelanotic and present as a CDCM. In addition, it reminds ophthalmologists of the necessity of systemic work-up of CM patients, including the important role of SNLB in detecting subclinical, regional spread of the disease in some cases.

History

A 49-year-old man was referred to the Cornea and Ocular Oncology clinics at the Byers Eye Institute at Stanford University for a amelanotic corneal mass. He had a history of recurrent left conjunctival melanoma (CM) and primary acquired melanosis (PAM) that were treated over the prior 13 years with excisional biopsies, cryotherapy, absolute alcohol, and two cycles of topical mitomycin C. His last treatment was 4 years ago. He had no other significant past medical history.

Examination

On examination, his BCVA was 20/20 and 20/25 in the right and left eyes, respectively. Right and left IOP measurements were 16 and 14 mmHg, respectively. Anterior segment exam of the left eye revealed vascularized, elevated amelanotic corneal mass measuring 5 mm x 3.75 mm (**Figure 1A**). With eyelid eversion, no pigmented conjunctival lesions were noted (was there scarring from past surgery?). Anterior segment exam of the right eye and fundus exam of both eyes were normal. Anterior segment OCT ((Visante™ OCT (Zeiss Meditec, Dublin, CA)) of the left eye demonstrated raised hyperreflective mass distinct only on the surface of the cornea measuring: 4.73 mm (base) and 1.19 mm (thickness) with no evidence of stromal or intraocular invasion (**Figure 1B**).

Discussion and Diagnosis

Malignant CM is a rare ocular surface malignancy that has an incidence of 0.2 - 0.8 per million per year and typically occurs in adults at a median age of 62 years.^{1 2 3 4 5} About 70% of CM arises from PAM, an acquired flat, patchy pigmentation of the conjunctiva with irregular margins, but it can also arise from a pre-existing nevus or de novo.^{6 7 4} Clinically, PAM lesions with more than 3 clock hours involvement of the conjunctiva, extension onto the cornea, nodular, multifocal, or vascular appearance have higher risk for progression to CM.⁷ On histopathology, PAM is identified as abnormal intraepithelial melanocytes that can have different levels of atypia. While conjunctival PAM without atypia is benign, conjunctival PAM with atypical melanocytes has 46%-90% risk of progression to CM.^{8 9 10 7 4} Conjunctival melanoma

shows substantial clinical variability but classically presents as a pigmented, elevated, sometimes nodular, conjunctival lesion; prominent feeder vessels with surrounding flat PAM may be present.^{8 11 4} Of note, CM and predisposing PAM may occur on the bulbar, forniceal or tarsal conjunctiva stressing the importance of a thorough examination with lid.⁴ However, 15-20% of CM can be amelanotic and may show extension or secondary recurrence onto the cornea—a rare manifestation called a corneally displaced CM (CDCM).^{12 13 14 15}

The management of CM and PAM with atypia varies based on the extent of the lesion. We and others⁵ favor aggressive treatment of small conjunctival lesions with wide margin excisional biopsy using a “no touch technique” and adjuvant cryotherapy to the margins.^{5 4} Larger lesions require map incisional biopsy and lamellar sclerectomy to confirm no scleral invasion⁵. Any corneal component is removed by absolute alcohol epitheliectomy and blunt dissection.⁵ Primary closure of surgical defects may be supplemented by large conjunctival rotational flaps, mucous membrane autografts, or amniotic membrane transplantation.^{5 4} We favor pathology review by an experienced ophthalmic pathologist and based on margin status and extent of disease, topical chemotherapy (e.g., mitomycin C or interferon-alpha-2B) may be considered. It is important to monitor for signs of regional or distal metastatic disease with repeated orbital and body scans and occasional consideration of SLNB.^{5 16 17}

Our patient had a history of left conjunctival melanoma that was excised 13 years prior to his presentation by an outside ophthalmologist. He presented to our institute 6 years later with increased flat pigmentation of the left bulbar conjunctiva temporally (**Figure 1C**), which was diagnosed as PAM with atypia on excisional biopsy and treated with 4-weeks, with an intervening 2-week break, of topical mitomycin C (**Figure 1D**). Two years later, he returned with recurrent flat pigmentation of the left bulbar conjunctiva temporally along the limbus with extension onto the cornea (**Figure 1E, F**). Excisional biopsy, absolute alcohol treatment, and amniotic membrane transplantation were performed (**Figure 1G**). However, pathology was not diagnostic due to crush artifact. One year later, he returned with increased flat conjunctival pigmentation along the superior limbus with minimal extension onto the cornea (**Figure 1H**). Excisional biopsy showed nodular conjunctival melanoma and PAM with atypia. Therefore, he underwent wide and extensive tumor excision, absolute alcohol treatment, cryotherapy, and amniotic membrane transplantation followed by a 4-weeks course of topical mitomycin C (**Figure 1I**). After failing to follow-up for 4 years, he presented with a vascularized, elevated amelanotic corneal mass (**Figure 1A, B and 2A, B**) consistent with a CDCM on wide excision of corneal and conjunctival base lesion, map biopsy and cryotherapy. In addition, he had lamellar sclerotomy to confirm clear margins, amniotic membrane transplantation (**Figure 2C, D**), and SLNB which failed to identify any pathologic nodes. Furthermore, he had complete metastatic work-up, including PET and MRI scans of the brain, chest, abdomen, and pelvis, which were all negative with 18 months of follow-up. **Figure 3** summarizes the timeline of our patient presentation.

Treatment of CM can be, as presented in our patient, challenging due to its high recurrence rate, despite excellent microscopic excision of the lesion, which can develop from associated PAM in 26% of patients by 5 years and 65% of patients by 15 years.^{5 4} Importantly, recurrent lesions are more often lightly pigmented compared to primary lesions and topical chemotherapy can increase the risk of depigmentation of the recurrent lesion, which decreases the ability to recognize amelanotic recurrence.¹⁵ The two cycles of topical mitomycin C treatment in our patient most likely contributed to depigmentation of his recurrent amelanotic lesion. In addition to local recurrence, CM can show distant metastasis, most commonly to ipsilateral facial lymph nodes, brain, lung, and liver.⁵ Conjunctival lymph channels generally drain toward the submandibular and preauricular superficial parotid nodes and the 10-year cumulative incidence of lymphatic spread is about 29%.^{5 4} Sentinel lymph node biopsy allows early detection of subclinical, regional spread of disease before it can be detected by other modalities, which provides an

earlier opportunity to treat metastatic disease.^{5 16 17} Therefore, SNLB has had an increased role in the management of CM over the past few years, especially for high risk lesions (e.g., thicker than 2 mm, nonlimbal location, diameter >10mm, recurrent disease, and histologic ulceration of the tumor).¹⁶ In addition, frequent screening for metastatic disease is essential.⁵

Conclusion

Malignant CM is a rare ocular tumor with an aggressive course resulting in high risk of recurrence. Sometimes these recurrences can be amelanotic, compared to the primary tumor, and, as in our unusual case, present as a CDCM. Management of CM and PAM with atypia can be challenging due to its high recurrence rate and the amelanotic nature of some recurrent lesions. Importantly, topical chemotherapy can increase the risk of depigmentation of the recurrent lesion. Treatment options varies based on the extent of the lesion and SNLB plays an important role in detecting subclinical, regional spread of the disease.

Figure 1

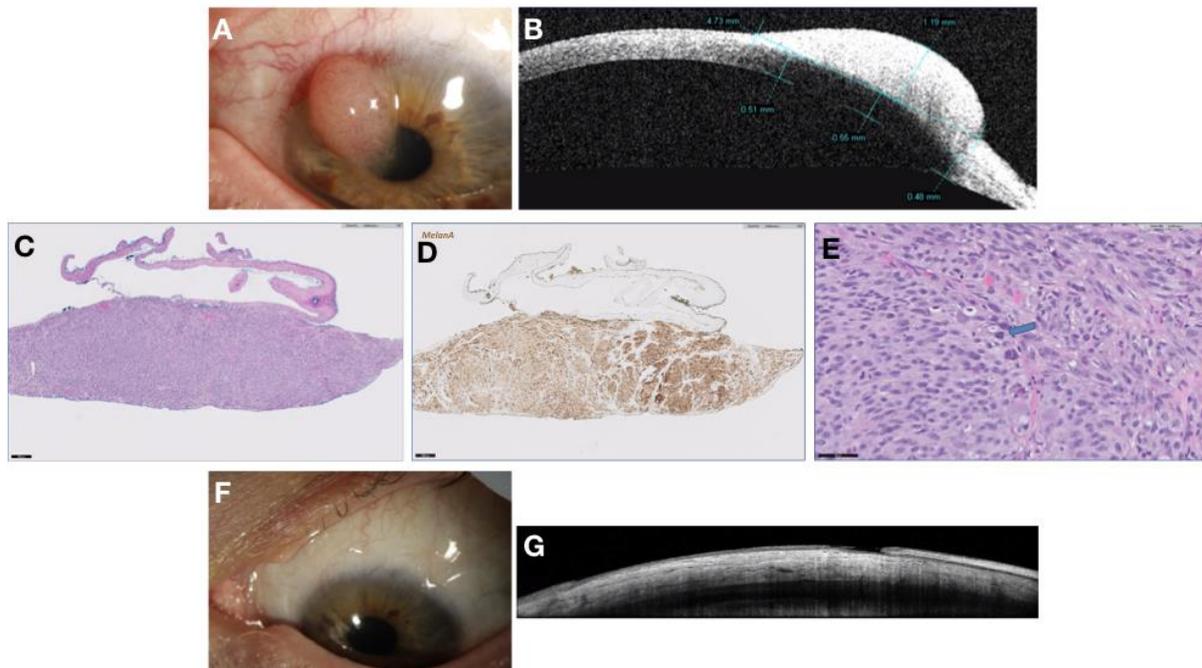


Figure 1. Slit lamp photo of the left eye showing a vascularized raised amelanotic corneal mass measuring 5 mm x 3.75 mm before (A) and after (F) treatment. Anterior segment OCT photo showing raised mass on the cornea measuring: 4.73 mm (base) and 1.19 mm (thickness) with no evidence of stromal invasion before (B) and after (G) treatment. (C) Hematoxylin and eosin-stained section of the

corneal lesion in (A) showing malignant melanocytes. (D) Melan-A staining showing melanoma cells expressing Melan-A (a surface protein that is expressed on of melanocytes). (E) high-power photo of the section in (A) showing atypical malignant melanocytes, including a big mitotic figure (arrow).

Figure 2

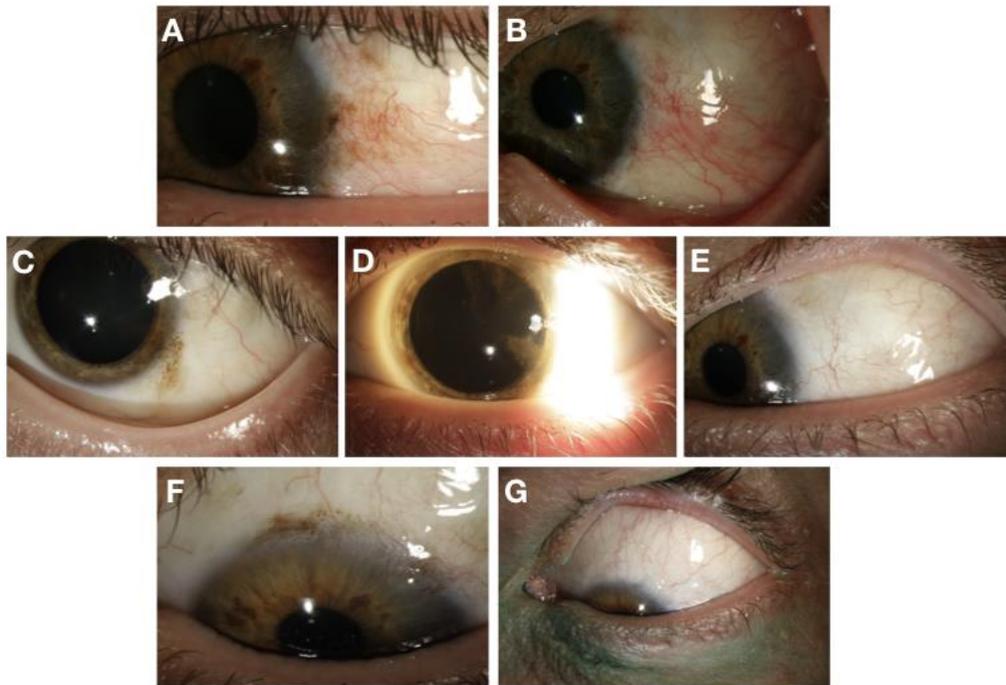


Figure 2. Slit lamp photo of the left eye in 2011 showing flat pigmentation of temporal bulbar conjunctiva before (A) and after (B) treatment. Slit lamp photo of the left eye in 2013 showing flat pigmentation of the bulbar conjunctiva temporally along the limbus with extension onto the cornea before (C, D) and after (E) treatment. Slit lamp photo of the left eye in 2014 showing flat conjunctival pigmentation along the superior limbus with minimal extension onto the cornea before (F) and after (G) treatment.

Figure 3

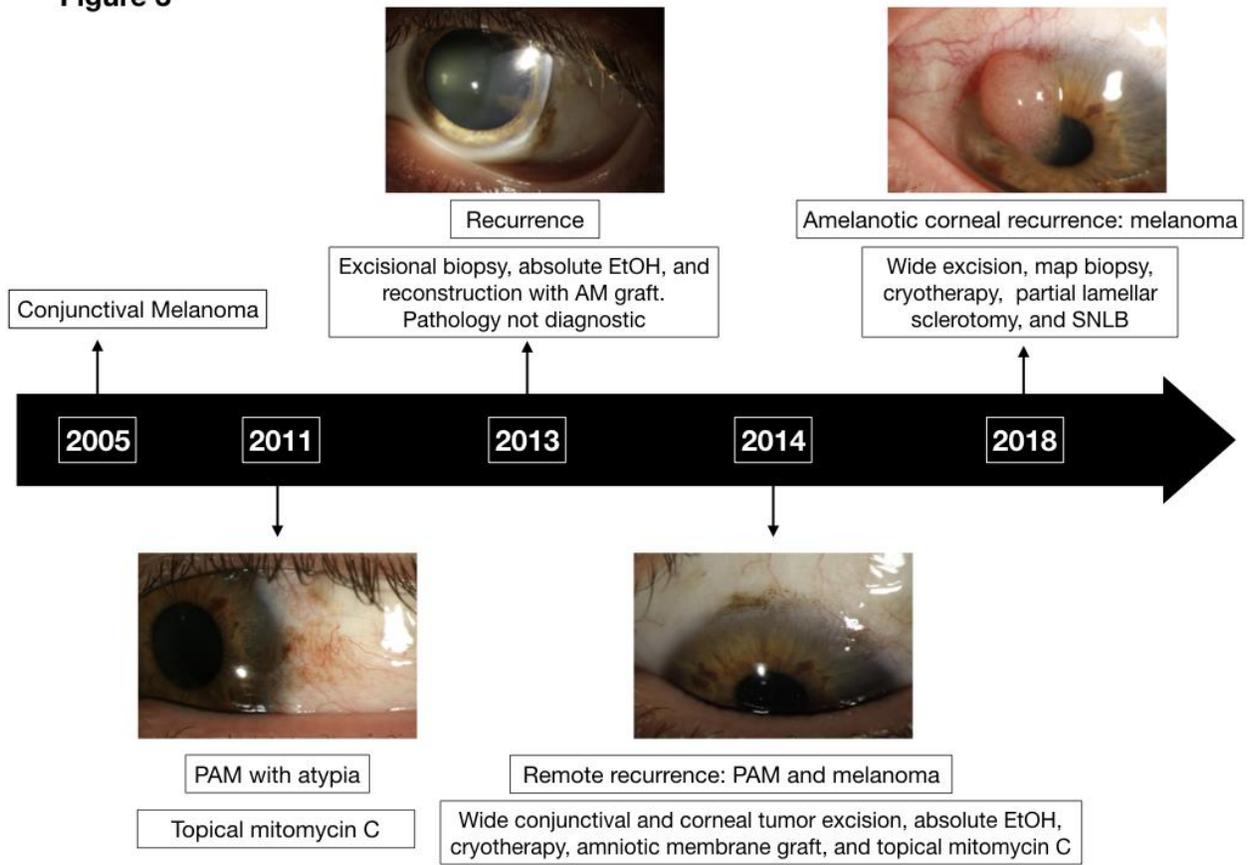


Figure 3. Timeline of the clinical course of the patient.

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