# Malignant conjuctival melanoma from primary acquired melanosis

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## Introduction

Melanoma is a malignant pigmented lesion with a prevalence of approximately 1 per 2 million in European population. Conjunctival melanomas make up less than two percent of all ocular malignancies. They are rare in black and Asian population. Melanocytic tumors of conjunctiva range from benign nevi and primary acquired Melanesia (PAM) to invasive malignant melanomas (MM).[1] Wereporta 54 year old male with multi-focal conjunctival pigmented lesion in the background of diffuse PAM. Incisional biopsy confirmed the diagnosis of conjunctival malignant melanoma.

## Case History

A 54yearold gentleman referred to the oculoplastic clinic with complaint of left lower conjunctival swelling since one week. There was no history of trauma, infection or inflammation prior to this problem. His previous ocular and medical history were not significant.On examination his uncorrected visual acuity was 6/12 corrected to 6/6 with -0.25-0.75.5X125 in right eye and 6/6 in left eye. Intraocular pressure measured 22mmHg and19 mmHg in right and left eyes respectively. Extraocular movements were full in all fields of gaze. Slit lamp examination revealed unremarkable anterior and posterior segments in the right eye. The left eye showed diffuse black nodular lesion involving inferior forniceal area, extending from caruncle to the lateral aspect ofconjunctiva measuring11mm x 5mm.

**Fig. 1**

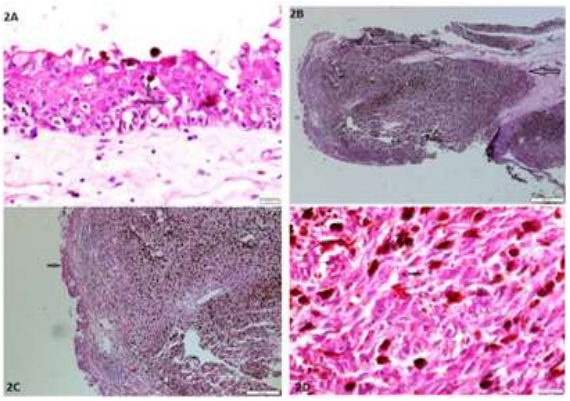


**Fig. 2**

There are patches of grey-black discoloration involving the inner part of lower eyelid as well as the supero-nasal area of the conjunctiva. The anterior segment and dilated fundus exam were completely normal. There was no lymph node involvement in head and neck region.

The lesion is highly suspicious of a multi focal conjunctival melanoma in the background of diffuse PAM. Incisional biopsy was done and sent for histopathology. The affected specimen showed PAM with and without melanosis (Fig. 2A), heavy infiltration of pigmented melanoma cells in epithelial (Fig. 2B), sub epithelial and substantia propria(Fig. 2C). High magnification revealed intracellular melanin pigment and cells in mitotic division **(Fig. 2D).** Treatment options available for this patient is wide excision with cryotherapy and mitomycin C or wide **e**xcision with intraoperative frozen section margin and base controlled excision followed by ocular surface construction.

## Discussion

Two to twenty percent of Melanomas arise from a pre-existing nevus (functional or compound), while 70% arise from PAM and de novo tumors form 10%.[1] Primary melanomas as such are uncommon which is in our patient who had prior PAM. Not all pigmented tumors of conjunctiva are dark; twenty five percent of conjunctival melanomas are hypomelanotic or even amelanotic.[2] Amelanotic tumors may not necessarily be colorless, they may present as a pink, fleshy mass, creating diagnostic problems. Such tumors are likely to be mistaken for tumors of the stratified squamous

epithelium. In our case, the lesion was pigmented. Primary acquired melanosis of conjunctiva is very common. Gloor P. has reported over one third of patients to have at least one patch of conjunctival melanosis in at least one eye.[3] PAM patches are usually limited in extent and become worrisome in persons of older age group. Also common are melanocytic nevi of the conjunctiva, and may be congenital or acquired. PAM typically appears as a flat patch-like lesion in the interpalpebral fissure, most frequently adjacent to the limbus. Focal thickenings within melanotic PAM appear darker than thinner portion of PAM and such foci are highly suspicious for malignant transformation. Lesions that are large, multifocal, darkly melanotic, or progressive during short-term observation and those involving unusual locations such as fornix, semilunar folds, caruncle, palpebral conjunctiva and extra-limbal bulbar conjunctiva are highly suspicious for clinically significant premalignant PAM.[4] Our patient had almost all such features (Fig. 1). Such lesions are always recommended for biopsy or excision, as was done in our patient. Melanocytic tumors of the conjunctiva affect individuals of all races and both sexes. Benign melanocytic tumors predominate in less than or 20 years age group, while premalignant such as PAM and malignant tumors such as MM predominate in older individuals. Recognized risk factors for premalignant and malignant lesions include white race, older age and exposure to intense and repeated sunlight. Our patient is of white race and has a very well-known history of exposure to sunlight due to his outdoor activities. Transformation of conjunctiva nevi to malignant form is uncommon; in contrast transformation of PAM to malignant variant is relatively common.[5] Presence of atypical melanocytic hyperplasia within PAM is a strong predictor of malignant change. Rarely underlying ciliary body melanoma can extend through sclera and present like a conjunctiva melanoma.

Conjunctiva melanoma, though less common than squamous cell carcinoma has an annual incidence of 2 to 4 new cases per 10 million persons in white population per year. Its cumulative lifetime incidence in whites is approximately 1 in 50,000 to 75,000 persons, and the frequency in blacks is eight times lower.[4] Presentation is in 6$^{th}$ decade except in patients with dysplastic nevus syndrome who develop multiple melanomas earlier.Atypical malignant melanoma of the conjunctiva appears as a focal nodular melanotic epibulbar mass, with multiple prominent epibulbar blood vessels extending to and from the lesion and involving the mass. Due to heavy vascularization, these tumors may bleed easily. Limbal area in interpalpebral fissure is the most common site for conjunctiva malignant melanomas arising de novo, however, those arising from PAM can develop from any portion of the lesion, including the fornices, palpebral conjunctiva and cornea.[6] The nodular melanoma can measure ≤3mmto≥10mm in diameter and ≤1mm to ≥3mm in thickness. The tumor mass in our patient measured 11mm x 5mm. Tumors in hidden locations like fornices and superior bulbar areas are likely to be larger when diagnosed first. Conjunctiva melanomas have strong propensity to metastasize, initially to pre-auricular or anterior cervical lymph nodes.[7,8] Intra-lymphatic spread has high risk of metastasis.Large size of the tumor, forniceal location and caruncular involvement are prognostic of lymph node involvement. Our patient had forniceal and caruncular involvement but no lymph node involvement.

Factors that influence the mode of treatment include the size and location of the tumor, presence or absence of regional lymphadenopathy and distance metastasis, presence or absence of associated PAM, age of the patient, systemic condition of the patient and any prior attempted excision of the tumor.[8] Conjunctiva nevi that are congenital or juvenile are least likely to undergo malignant transformation, those arising in early adolescence have somewhat higher rate of malignant transformation especially if they increase in pigmentation, size or thickness, and conjunctival nevi arising in adults have highest risk of malignant transformation.[9] Such lesions should always be excised without any delay.

Malignant melanoma of conjunctiva, in general, has better prognosis than cutaneous melanoma. Overall mortality rate is 25% and death from metastatic disease following initial diagnosis and treatment of primary conjunctiva melanoma is 15-20% after 5 years,25-30% after 10 years, 30-35% after 15 years.[8] Poor prognostic factors include thickness more than 1.8mm, involvement of eyelid margin, pagetoid or full thickness intraepithelial spread, lymphatic invasion and mixed-cell type. Conjunctiva malignant melanomas are potentially deadly tumors with metastasis in 26% and death in 13% of patients ten years after surgical excision. A well planned follow up is mandatory for all such patients. Gene expression profiling is currently being evaluated to determine prognosis and might be beneficial in the future to determine response to targeted chemotherapies that are under development. Our patient has a very short follow up yet and needs a regular follow up for years.

In conclusion, conjunctiva melanoma carries high risk of developing metastasis, prompt excision or other specified treatment is strongly advocated. Patient in this case report has high risk factors like white skin, exposure to sunlight and size of the tumor but bears a better prognosis due to non-involvement of lymph nodes and absence of distant metastasis.

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