

Conjunctival Malignant Melanoma: Report of A Rare Case

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ABSTRACT

Ocular melanomas comprise 3.7 percent of all melanomas. Amongst ocular structures, melanoma of conjunctiva is an uncommon tumor and comprise around 5 percent of the melanomas in the ocular region. Non-bulbar conjunctival malignant melanomas (CMM) are rare and are associated with substantial morbidity and mortality. As the presentation varies, clinical diagnosis is missed in the early stages. When CMM are amelanotic, differentiating them from other epithelial lesions on the basis of morphological features becomes even more difficult. High index of suspicion on the part of histopathologist can achieve early diagnosis of CMM on the basis of characteristic biopsy findings. Confirmed diagnosis on the basis of histopathological examination (HPE) and immunohistochemistry (IHC) studies can lead to appropriate timely management in these cases.

Keywords: Malignant Melanoma, Conjunctiva, Amelanotic, Histopathology Diagnosis.

Introduction

Amongst ocular melanomas, uvea is the most frequent site of occurrence (83%), while conjunctiva is the less common site for the occurrence of malignant melanoma (MM) (5%)^[1]. In conjunctival melanomas, bulbar conjunctiva is commonly involved and noticed early. Tarsal/palpebral conjunctiva is rarely involved by the neoplasm^[2]. Conjunctival malignant melanomas (CMM) are known to occur in the background of pigmented lesions as in primary acquired melanosis in fifty-seven to seventy-six percent cases and less commonly arise *denovo* (16-25%) or from nevi (1-6%)^[2,3]. Melanomas are amelanotic in 15-19% of cases, especially those occurring *denovo* and are often mistaken with epithelial malignancies which are of more common occurrence at that site^[4,5]. Reports about CMM are lacking in Indian literature^[6]. We report a case of CMM, in an old patient of Asian ethnicity, occurring in tarsal conjunctiva. Diagnosis in this case was made on the basis of histopathological examination (HPE) findings in an orbital exenteration specimen.

Case Report

A 75 years female patient came to ophthalmology outpatient-department with the complaints of diminution of vision in both eyes for four months. She also complained of increase in size of left eye with difficulty in closing the eye completely since two months. The eye enlargement was progressive and painless. There was no history of watering from eyes, photophobia or bleeding from swollen left eye. There was no history of trauma. Patient is a known hypertensive and is on medication for the same. She

suffered cerebrovascular episode 10 years back from which she recovered completely. There is no history of diabetes mellitus, asthma, previous ocular complaints or spectacle use. Patient belongs to Asian ethnicity and was farmer by occupation. She is average built, alert, with stable vitals. Her systemic examination was within normal limits.

On ocular examination, diminution of vision in both eyes was attributed to immature senile cataract. A mass-lesion of 3x2cm was present near the inner canthus causing improper closure of left eye (**Fig. 1A**). It was over the posterior surface of left upper eyelid, away from the lid margin and covering medial two-thirds of the eyeball (**Fig. 1B**). Eyeball was displaced laterally causing restriction of ocular movements. The mass was retractable and separate from underlying eyeball structures, with no intra-ocular extension (**Fig. 1C**).

In both eyes, cornea, anterior chamber, iris and pupil examination were within normal limits and bilateral lenses showed changes of cataract. Fundus examination was not possible owing to dense cataract in the left eye.

Orbital computerised-tomography (CT) revealed a hyperdense lesion along the antero-medial aspect of left eyeball, causing its displacement postero-laterally. Both eyeballs appeared normal in size with intact lenses, normal scleral-uveal thickness, normal extra and intra conal structures, with usual attenuated vitreous for the age. Normal bilateral lacrimal glands, extra-ocular muscles and optic nerves were noted. Both orbits were normal with no lytic or sclerotic lesion (**Fig. 1D**).

The left upper eyelid mass was biopsied with a clinical suspicion of malignancy. Biopsy was in multiple tissue bits. HPE of the H&E stained slide revealed features of epithelial malignancy.

Wide local excision of the eyelid growth was done along with left orbital exenteration. Reconstruction by split thickness skin grafting from left thigh was performed.

Left orbital exenteration specimen with tumor mass was received in histopathology section (**Fig. 2A**). Lid mass, of size 2.5 x 2 x 1.8 cms, was seen to be attached to the posterior surface of upper lid and was lying anterior to the eyeball. Cut-surface of the mass was firm in consistency and reddish-pink in color (**Fig. 2B**).

HPE of specimen revealed skin, tarsal plate structures and flattened conjunctival lining with a tumor mass beneath. Tumor was comprising of polygonal and spindle cells. The cells showed pleomorphic nuclei with prominent nucleoli and vacuolation in some nuclei. Brisk mitotic activity and tumor giant cells were noted. Focal areas revealed intra as well as extra-cellular coarse, brown-black pigment identified as melanin. There was no evidence of lymphovascular and perineural invasion.

HPE features suggested epithelial malignancy--- favoring diagnosis of malignant melanoma (MM). Masson-Fontana stain confirmed the presence of melanin in the tumor. HMB-45, a specific IHC marker for melanoma, confirmed the diagnosis of MM (**Fig. 3A and 3B**).

All surgical margins and left optic nerve were free from tumor infiltration. HPE of whole of the eyeball did not reveal involvement of uveal structures. Gross and microscopic features of the orbital exenteration specimen suggested primary origin of MM from tarsal conjunctiva.

Also, thorough clinical and radiological examination revealed no evidence of pre or post auricular and cervical lymphadenopathy, nor any organomegaly. Chest-radiograph was normal. There was no evidence of any cutaneous or oral pigmented lesion.

Taking into consideration all the clinical, radiological, HPE and IHC findings, final diagnosis in our case was Primary Malignant Melanoma of Tarsal conjunctiva -- pT2c N0 M0. No stage grouping is presently recommended by AJCC^[7]. As the present case appeared to arise denovo, patient carries a higher risk of metastasis and was advised post-operative radiotherapy. The patient has not reported to the radiotherapy unit till the filing of this report.

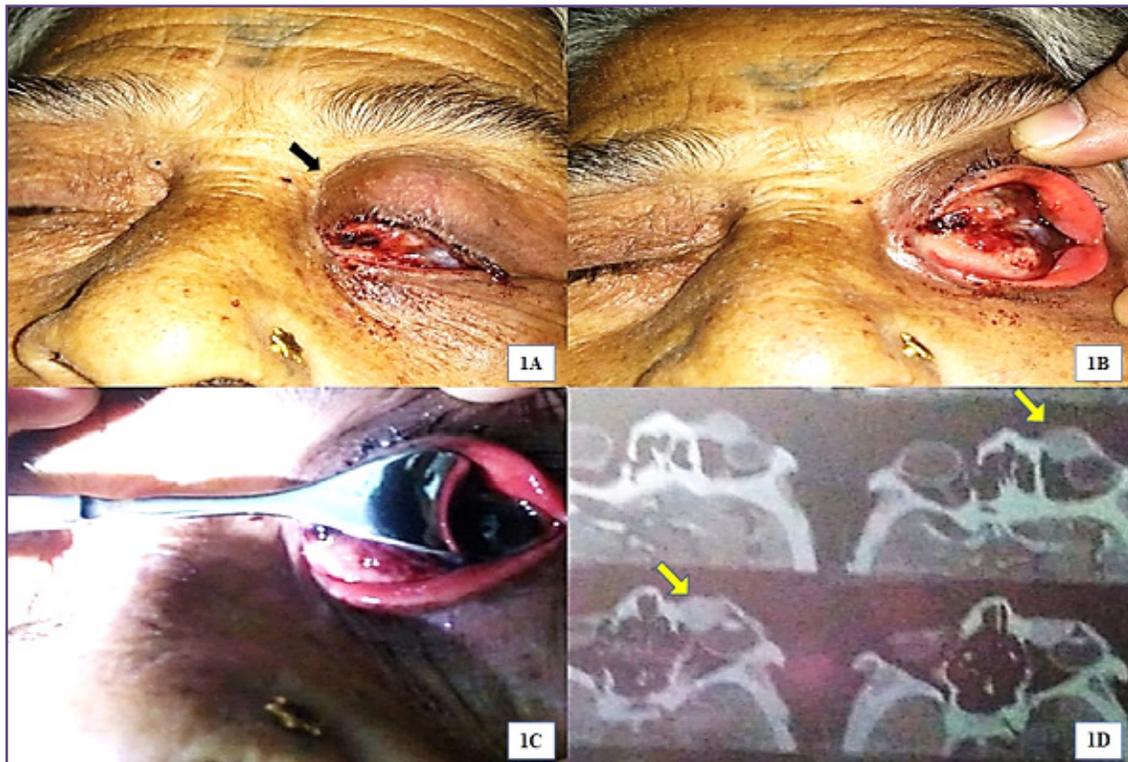


Fig. 1: (A) eyelid swelling causing improper closure of left-eye; (B) mass over posterior surface of left upper lid, away from lid margin; (C) retractable mass, separate from underlying eyeball structures; (D) CT orbits: hyperdense lesion along the antero-medial aspect of left-eyeglobe.

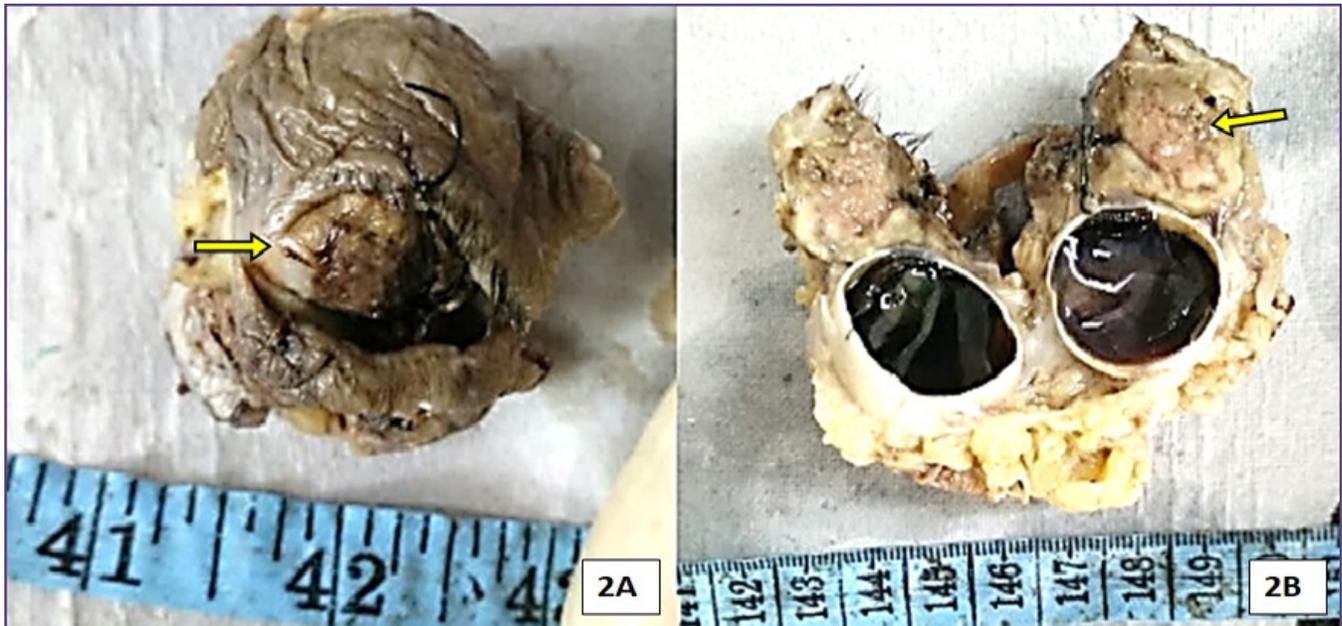


Fig. 2: Gross (A) Left orbital exenteration specimen with upper eyelid tumor mass; (B) Mass attached to the posterior surface of left upper lid and lying anterior to the eyeball. Cut surface of the mass was reddish-pink in colour.

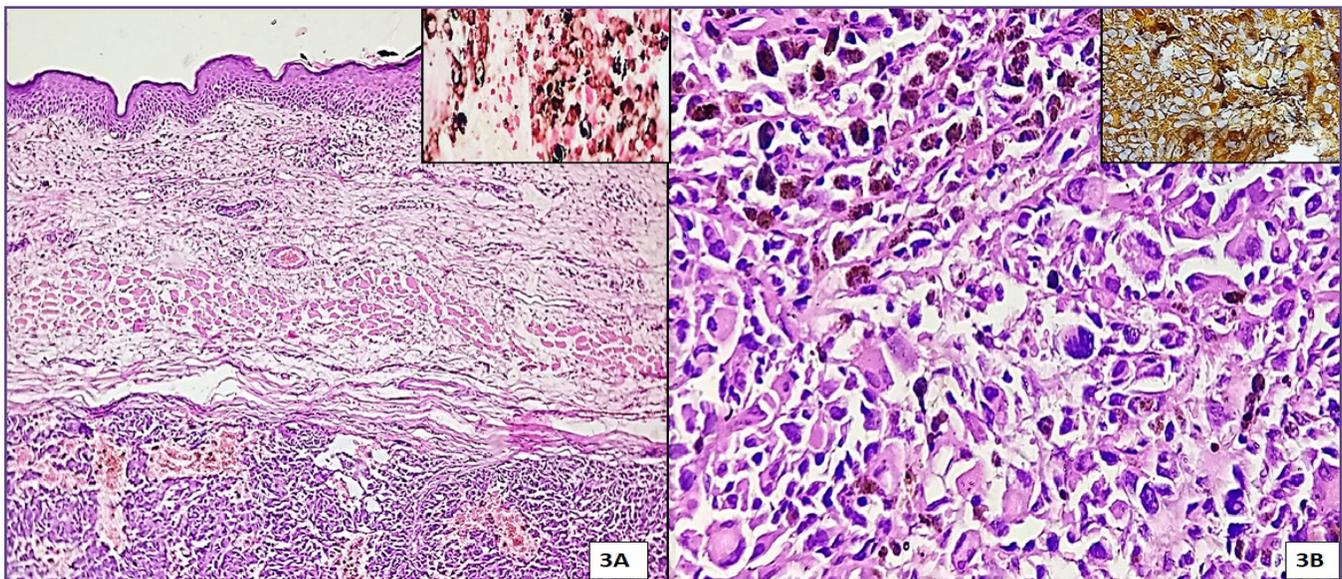


Fig. 3: Microscopy (A) HP- Skin, tarsal plate and thin conjunctival epithelium with underlying tumor (10x, H&E Stain), Inset: Masson-Fontana positivity. (B) HP- Atypical melanocytes with varying shapes and sizes, pleomorphic nuclei and focal intracellular melanin pigment (40x, H&E Stain), Inset: HMB-45 positivity.

Discussion

Melanoma is a malignant tumor of the melanin producing cells – melanocytes and it occurs at cutaneous and extracutaneous sites^[8]. Extracutaneous melanomas include tumors that occur at mucosal lining of respiratory, digestive and genitourinary tracts, also at the ocular, orbital, leptomeningeal sites, and metastatic MM^[9].

Ocular melanomas comprise 3.7% of all melanomas and is the most common primary extracutaneous tumor^[1]. They arise from the melanocytes situated in the uveal tract that includes choroid, ciliary body, iris and also from the melanocytes in orbit, eyelids and basal layer of conjunctival epithelial membrane^[10].

CMM accounts for 5% of melanomas in the ocular region and 0.25% of overall melanomas^[1,8]. The mean age of presentation of CMM is usually in the sixth decade, but cases occurring in children are also on the record^[11]. Some studies have shown a greater association with male gender. Amongst ethnic groups, Asians are the least affected and whites show higher incidence than blacks^[8].

The development of CMM lacks an association with sun damage, family history or precursor nevi^[12]. However, associations with primary acquired melanosis with atypia and nevi have been reported. CMM are also known to arise de novo^[3]. Bulbar conjunctiva is the most common location for melanotic tumors and often occupies the limbus^[9]. In conjunctiva, the less common locations include palpebral and forniceal conjunctiva, plica semilunaris and caruncle^[4].

CMM commonly presents as unilateral, thickened, raised, pigmented lesion and less often as yellow-pink nodule^[10]. There can be associated ocular pain and irritation. Conjunctival melanomas are mostly pigmented lesions, but 15-19% are amelanotic (with variable or no pigment)^[3]. Amelanotic CMM have to be differentiated from varied benign and malignant lesions^[4,5]. Present case was initially diagnosed as epithelial malignancy on incisional biopsy because of sparse melanin pigment in the tumor.

Clinical examination and slit-lamp findings are the basis of clinical diagnosis of CMM. Various imaging modalities such as USG, CT, MRI and PET scan also help in evaluation of the ocular melanocytic lesions which affect the conjunctiva^[12].

The present case of CMM, that has originated from an uncommon site of palpebral conjunctiva, denovo, in a female of Asian ethnicity, is thus rare in many aspects. Our patient has higher chances of metastasis and carries poor prognosis.

On HPE, atypical melanocytes may exist in variable forms like spindle cells, balloon cells, polyhedral cells, round-epithelioid cells and bizarre-multinucleated cells. These cells are located in the lining mucosa and substantia propria. The amount of melanin varies from tumor to tumor. Abundant melanin may at times obscure the cell morphology or, it may be scant and can be seen focally. IHC markers like HMB-45, Melan-A, S-100 aid in the diagnosis of MM. There is no single criteria for histopathological diagnosis of melanoma of conjunctiva. Combined findings of atypical melanocytic cells in the epithelium, atypical mitoses, invasion of tumor in subepithelial tissue and plasma-lymphocytic inflammatory response at periphery of tumor are the major histologic features that favor diagnosis of MM^[11,13].

Local recurrences are common in CMM. Lymphatic and hematogenous spread are known to occur in CMM. Most affected lymph nodes are pre-auricular, submandibular and deep cervical groups^[10,14]. Organs affected by hematogenous spread are liver, lungs, brain and skin^[9].

TNM classification of CMM is as per the AJCC guidelines which describes stage-T1 as affecting the bulbar conjunctiva, while tumors affecting non-bulbar sites (palpebral and forniceal conjunctiva and caruncle) are placed in stage-T2^[7].

Current management of CMM is wide local excision of growth or exenteration of the affected eyeball. Although less sensitive, the adjuvant therapies include topical chemotherapy, cryotherapy and radiotherapy^[4].

Clinical factors associated with unfavorable prognosis in CMM are location at non-bulbar sites that are associated with late diagnosis and early metastasis; and multifocal lesions. Histopathological factors associated with worse prognosis are 1) thickness (depth) > 2mm, 2) mixed cell type of lesions, 3) pagetoid spread, 4) atypical mitoses, and 5) absence of inflammatory response^[5,14].

Conclusion

Although rare, CMM should be considered in the differential diagnosis of both pigmented and non-pigmented eye lesions. Early detection of conjunctival melanoma by HPE can lead to timely management of the aggressive lesions.

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