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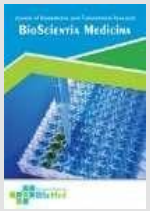

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Malignant Transformation of Primary Acquired Melanosis into Conjunctival Melanoma in an Adolescent Male: A Clinico-Pathological Case Report and Management Review

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A B S T R A C T

Background: Conjunctival malignant melanoma (CMM) is a rare but potentially lethal ocular surface malignancy, especially uncommon in adolescents. It often arises from a precursor lesion known as primary acquired melanosis (PAM) with atypia. We present a case of CMM developing from long-standing PAM in an 18-year-old male, highlighting the diagnostic and therapeutic challenges in this unusual demographic. **Case presentation:** An 18-year-old male presented with a pigmented conjunctival lesion in his right eye, which had been present for over a decade but had recently shown progressive enlargement and darkening. Slit-lamp biomicroscopy revealed a 5x2 mm, variegated, hyperpigmented lesion on the bulbar conjunctiva with a prominent feeding vessel. The patient underwent an excisional biopsy using a "no-touch" technique with 4 mm margins and adjunctive double freeze-thaw cryotherapy. Histopathological analysis confirmed an invasive malignant melanoma, Breslow thickness of 1.8 mm, arising from PAM with severe atypia. Surgical margins were clear of the tumor. **Conclusion:** This case underscores that malignant transformation of conjunctival melanocytic lesions can occur even in young patients. The presence of a changing pigmented lesion, regardless of patient age, necessitates a high index of suspicion and a low threshold for excisional biopsy. Meticulous surgical technique combined with adjuvant therapy and vigilant long-term surveillance is paramount for optimizing patient outcomes.

1. Introduction

Malignant melanoma, a neoplasm originating from the malignant proliferation of melanocytes, can manifest in any anatomical location where these pigment-producing cells reside.[1] While cutaneous melanoma is the most widely recognized form, melanomas arising from mucosal surfaces, including the conjunctiva, represent a distinct and more aggressive clinical entity. Conjunctival malignant melanoma (CMM) is a rare ocular surface malignancy, accounting for a mere 2–5% of all ocular melanomas and approximately 0.25% of all malignant melanomas.[2] Despite its rarity, CMM is associated with significant morbidity and mortality, with reported 10-year mortality rates reaching up to 30%, primarily due to metastatic dissemination.[3]

The incidence of CMM, though low, has demonstrated a concerning upward trend over the past several decades, particularly in fair-skinned populations. Data from the Surveillance, Epidemiology and End Results (SEER) program in the United States indicated a doubling in incidence from 0.22 cases per million per year during 1973–1979 to 0.46 cases per million per year in the 1990s, a trend that has continued. This rise is strongly linked to environmental factors, with chronic exposure to

ultraviolet (UV) radiation being the most well-established etiological risk factor, analogous to its role in cutaneous melanoma.[4]

The developmental pathway of CMM is heterogeneous. It can arise de novo from apparently normal conjunctiva (approximately 25% of cases), from a pre-existing benign conjunctival nevus (around 5% of cases), or, most commonly, from a precursor lesion known as primary acquired melanosis (PAM).[5] PAM is responsible for up to 75% of CMM cases. PAM is a clinical term describing a spectrum of acquired, flat, and often patchy areas of conjunctival pigmentation.[6] Histopathologically, it is classified based on the absence or presence of melanocytic atypia. While PAM without atypia is a benign condition characterized by a simple increase in melanin production or a benign proliferation of normal melanocytes, PAM with atypia involves a proliferation of atypical melanocytes within the basal layer of the conjunctival epithelium and is considered a true pre-malignant lesion.[7] The risk of malignant transformation of PAM with atypia into invasive CMM is significant, estimated to be between 13% and 50%, depending on the severity of the atypia.[8]

The diagnosis and management of CMM pose unique challenges. Clinically, it often presents as a pigmented, elevated nodule on the bulbar conjunctiva, frequently with prominent feeder vessels. However, its appearance can be highly variable, with some lesions being minimally pigmented (amelanotic), diffuse, or multifocal, complicating the differential diagnosis which includes benign nevi, racial melanosis, and secondary pigmentation. The current standard of care for localized CMM involves wide local surgical excision using a meticulous "no-touch" technique to prevent iatrogenic tumor seeding, often combined with adjuvant therapies such as cryotherapy, topical chemotherapy (Mitomycin C, Interferon α2b), or plaque radiotherapy to eradicate microscopic residual disease and reduce the high rates of local recurrence.

While CMM is predominantly a disease of the elderly, with a peak incidence in the sixth and seventh decades of life, its occurrence in children and adolescents is exceptionally rare.[9] This rarity can lead to a lower index of suspicion among clinicians, potentially delaying diagnosis and treatment in younger populations. A long-standing pigmented lesion in a young individual is often presumed to be a benign nevus, yet any documented change in size, shape, or color should prompt immediate and thorough evaluation.[10]

This case report aims to detail the clinical presentation, histopathological findings, and management of a biopsy-confirmed CMM arising from PAM with atypia in an 18-year-old male. The novelty and educational value of this case lie in its occurrence within an unusual age demographic, reinforcing the critical oncologic principle that any changing pigmented lesion warrants histopathological assessment, regardless of the patient's age. We aim to underscore the importance of early diagnosis, methodologically rigorous surgical intervention, and the necessity of long-term multidisciplinary surveillance for this rare but life-threatening condition.

2. Case Presentation

An 18-year-old male of Indonesian ethnicity was referred to the Ophthalmology Clinic at Dr. M. Djamil General Hospital, Padang, for evaluation of a growing pigmented lesion in his right eye. The patient reported that a small, flat, brown spot had been present on the white of his eye for as long as he could remember, at least for the past 10 years. He stated that the lesion had been stable and asymptomatic for most of his childhood, resembling a simple "mole." However, over the preceding three years, he noted a gradual but definite change in its characteristics. The lesion had become progressively larger, darker in color, and its surface had transformed from flat to slightly raised and irregular (Table 1a and 1b).

He denied any associated symptoms such as pain, itching, foreign body sensation, discharge, excessive tearing, or changes in vision. His medical history was unremarkable, with no known chronic illnesses like diabetes mellitus or hypertension, and no history of

ocular trauma or prior ocular surgery. The patient's family history was negative for any form of cancer, including melanoma, or other significant inheritable eye diseases. Social history revealed that the patient was a student who engaged in frequent outdoor activities. He reported significant daily sun exposure and frequently rode a motorcycle without the use of sunglasses or other forms of eye protection, constituting a notable history of chronic UV radiation exposure. Written informed consent was obtained from the patient for the use and publication of his clinical data and accompanying images for educational and scientific purposes.

Table 1a. Patient Background and General Examination

Anamnesis and Physical Status on Admission

CATEGORY	PARAMETER	FINDING / DETAIL
Demographics	Age	18 years
	Gender	Male
	Ethnicity	Indonesian
History	Chief Complaint	Growing pigmented lesion in the right eye.
	History of Present Illness	Lesion present for >10 years; progressive enlargement, darkening, and elevation over the last 3 years. Asymptomatic.
	Past Medical/Ocular History	Unremarkable. No chronic illness, trauma, or prior surgery.
	Family History	Negative for cancer or significant eye disease.
	Social History	Frequent outdoor activities with significant unprotected sun exposure (no sunglasses).
General Examination	General State	Good state of health, compos mentis.
	Vital Signs	BP: 120/70 mmHg, HR: 86 bpm, RR: 19/min, Temp: 36.5°C. All within normal limits.
	Lymph Node Survey	**Negative for palpable preauricular, submandibular, or cervical lymphadenopathy.**

Table 1b. Ophthalmic Examination and Diagnostic Summary

Ocular Findings and Initial Workup

CATEGORY	PARAMETER	FINDING / DETAIL	
Ophthalmic Examination	Visual Acuity (BCVA)	20/20 in both eyes (OU).	
	Right Eye (OD) Lesion Location	Nasal bulbar conjunctiva, 3 o'clock position, 1 mm medial to the limbus.	
	OD Lesion Size	5 mm (horizontal) × 2 mm (vertical).	
	OD Lesion Characteristics	• **Color:** Variegated (dark brown, black, tan). • **Surface:** Irregular and nodular. • **Margins:** Indistinct and poorly defined. • **Vascularity:** Prominent, tortuous feeding vessel present. • **Mobility:** Mobile over underlying sclera.	
	Left Eye (OS) Examination	Within normal limits, except for mild conjunctival hyperemia.	
	Intraocular Pressure (IOP)	Normal in both eyes.	
	Extraocular Movements	Full and orthotropic.	
	Fundus Examination (OU)	Within normal limits. Sharp optic discs, normal vasculature, clear macula.	
Systemic Workup & Diagnosis	Laboratory Tests		Complete blood count and comprehensive metabolic panel all within normal ranges.
Imaging		Chest Radiograph: No evidence of metastasis.	
Provisional Diagnosis		**Conjunctival Malignant Melanoma, Right Eye.**	

On general physical examination, the patient was in a good state of general health, alert, and cooperative (compos mentis). His vital signs were all within normal limits: blood pressure of 120/70 mmHg, pulse rate of 86 beats per minute, respiratory rate of 19 breaths per minute, and a body temperature of 36.5°C. His body weight was 65 kg and height was 170 cm. There was no palpable preauricular, submandibular, or cervical lymphadenopathy on careful examination, suggesting no clinical evidence of regional metastasis.

Ophthalmic examination revealed a best-corrected visual acuity of 20/20 in both eyes. Extraocular movements were full and orthotropic in all fields of gaze. Slit-lamp biomicroscopy of the left eye was entirely within normal limits, aside from mild conjunctival hyperemia. Examination of the right eye revealed a prominent, solitary pigmented lesion located on the nasal bulbar conjunctiva at the 3 o'clock position. The lesion was measured with calipers at the slit lamp to be 5 mm in horizontal diameter by 2 mm in vertical diameter. It was situated 1 mm medial to the corneal limbus. The lesion exhibited significant variegation in pigmentation, with areas of dark brown and black intermixed with lighter tan regions. Its surface was irregular and nodular, with indistinct and poorly defined margins. A large, tortuous, dilated conjunctival blood vessel (feeding vessel) was observed entering the base of the lesion. The lesion was mobile over the underlying sclera and not fixed to deeper tissues. The remainder of the anterior segment examination was normal, including a clear cornea, a deep and quiet anterior chamber, a normal iris architecture, a round 3 mm pupil reactive to light, and a clear crystalline lens. Intraocular pressure was normal in both eyes. Dilated funduscopic examination of both eyes was unremarkable. The optic discs were sharp and well-defined with a cup-to-disc ratio of 0.3, the retinal vasculature was normal, and the macula and peripheral retina were free of pathology.

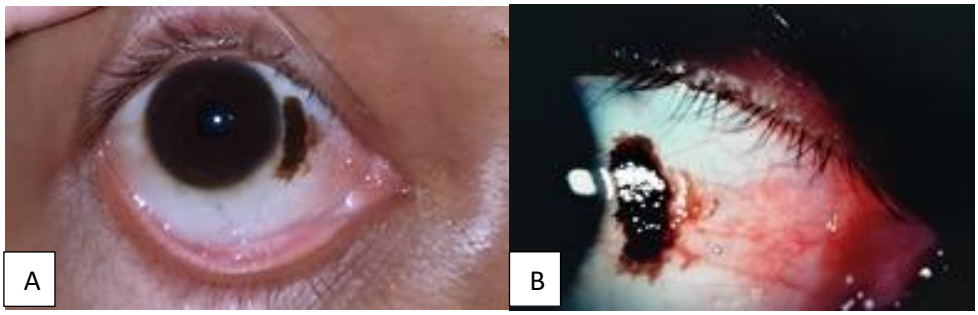

Figure 1. Clinical photographs of the patient's right eye at presentation. A) Gross clinical picture showing a prominent blackish lesion on the nasal conjunctiva. B) Slit-lamp photograph providing a magnified view of the 5x2 mm lesion, demonstrating its irregular surface, variegated pigmentation, and a large, tortuous feeding vessel.

Given the clinical features highly suspicious for malignancy—specifically, the documented history of change (evolution), irregular borders, color variegation, and the presence of a feeding vessel—a provisional diagnosis of conjunctival malignant melanoma was made. A comprehensive metastatic workup was initiated. Systemic blood investigations, including a complete blood count and comprehensive metabolic panel, were all within normal ranges. A chest radiograph was performed and revealed no evidence of pulmonary nodules, mediastinal lymphadenopathy, or pleural effusion, ruling out thoracic metastasis at the time of presentation. The decision was made to proceed with an excisional biopsy for definitive histopathological diagnosis and primary treatment.

Table 2. Therapeutic Intervention Summary

Surgical and Adjuvant Management Protocol

PHASE	PARAMETER	DETAIL / SPECIFICATION
Pre-Operative	Anesthesia	Local Anesthesia
	Asepsis	Sterile preparation and draping; ocular surface irrigation with Povidone-Iodine 5% solution.
Surgical Excision	Surgical Technique	**Wide Local Excision with "No-Touch" Technique.**
	Surgical Margins	**4 mm** of clinically uninvolved conjunctiva on all sides.
	Depth of Dissection	Dissection down to bare sclera, including removal of the underlying Tenon's capsule.
Adjuvant Therapy	Modality	Intraoperative Cryotherapy.
	Application Area	Applied to all conjunctival margins and the entire scleral bed post-excision.
	Technique	**Double Freeze-Thaw Cycles:** Two applications of freezing until ice ball visualization, followed by complete passive thaw.
Reconstruction & Closure	Closure Method	Direct closure of the conjunctival defect.
	Suture Material	Interrupted 6-0 Vicryl (polyglactin 910) sutures.
Specimen Handling	Orientation	Specimen oriented on a filter paper card with the limbal margin clearly marked for the pathologist.
	Fixation	Immediate placement in 10% Neutral Buffered Formalin.

The patient underwent surgery under local anesthesia. The procedure was performed with meticulous adherence to oncologic principles (Table 2). After sterile preparation and draping, the ocular surface was irrigated with a povidone-iodine 5% solution. The surgical plan involved a wide local excision utilizing a strict "no-touch" technique. This technique involves handling the lesion only by the surrounding healthy conjunctiva to prevent grasping the tumor itself, thereby minimizing the risk of intraoperative tumor cell seeding. The lesion was excised with a 4 mm margin of clinically uninvolved conjunctiva on all sides. The dissection was carried down to the bare sclera, ensuring complete removal of the lesion along with the underlying Tenon's capsule.

Following excision, adjunctive therapy was immediately applied. Double freeze-thaw cryotherapy was administered to the conjunctival margins and the scleral bed. A cryotherapy probe was used to apply two cycles of freezing until an ice ball was visualized, followed by a complete passive thaw. This step is critical for eradicating any potential microscopic

disease extension beyond the excision margins. The large conjunctival defect was closed directly with interrupted 6-0 Vicryl (polyglactin 910) sutures, with care taken to avoid excessive tension or forniceal shortening. The excised specimen was carefully oriented on a filter paper card, marking the limbal margin, and immediately placed in 10% neutral buffered formalin for transport to the pathology department.

Table 3. Histopathological Findings Summary

Microscopic and Quantitative Analysis

CATEGORY	PARAMETER	FINDING / DETAIL
General Findings	Macroscopic Examination	5×2 mm pigmented tissue fragment.
	Histological Diagnosis	**Invasive Conjunctival Malignant Melanoma.**
	Tumor Origin	Arising in the setting of Primary Acquired Melanosis (PAM) with severe atypia.
Tumor Characteristics	Cellular Composition	Nests and sheets of atypical melanocytes infiltrating epithelium and substantia propria.
	Cellular Morphology	Significant pleomorphism with a mix of epithelioid and spindle-shaped cells.
	Nuclear Features	Large, hyperchromatic, irregularly shaped nuclei with prominent eosinophilic nucleoli. High N:C ratio.
	Pigmentation	Variable, fine, dusty intracellular melanin pigment observed.
Quantitative Metrics	Tumor Thickness (Breslow)	**1.8 mm**
	Surgical Margins	**Negative for malignancy. Closest margin: 1.5 mm.**
	Mitotic Rate	2 mitoses/mm²
	Ulceration	**Absent**
	Lymphovascular Invasion	**Not identified.**
	Regression	Present (focal areas noted).
Final Diagnosis & Staging	Final Pathological Diagnosis	**Conjunctival Malignant Melanoma, invasive to a depth of 1.8 mm, arising in PAM with severe atypia.**
	AJCC 8th Edition Staging	**pT2a N0 M0**

The submitted specimen was analyzed by an experienced ocular pathologist. Macroscopic examination revealed a 5x2 mm pigmented tissue fragment (Table 3). Microscopic evaluation with Hematoxylin and Eosin (H&E) staining confirmed the diagnosis of an invasive conjunctival malignant melanoma. The analysis revealed nests and sheets of atypical melanocytes infiltrating the thinned conjunctival epithelium and invading the underlying substantia propria (stroma). The tumor cells exhibited significant pleomorphism, with a mix of epithelioid and spindle-shaped cells. These malignant cells were characterized by large, hyperchromatic, and irregularly shaped nuclei, prominent eosinophilic nucleoli, and a high nuclear-to-cytoplasmic ratio. Variable amounts of fine, dusty intracellular melanin pigment were observed throughout the tumor. The surrounding conjunctival epithelium showed features of primary acquired melanosis (PAM) with severe atypia, characterized by the confluent proliferation of atypical melanocytes along the basal layer, confirming the origin of the melanoma from a pre-existing PAM lesion.

Quantitative pathological analysis provided several key metrics crucial for prognosis. The maximum vertical thickness of the invasive tumor, known as the Breslow depth, was measured to be 1.8 mm. The surgical excision was successful, as the tumor was confirmed to be fully excised with the closest surgical margin located 1.5 mm from the invasive component. Microscopic assessment of cellular proliferation identified a mitotic rate of 2 mitoses/mm^2. Several favorable prognostic indicators were confirmed: ulceration was absent, and there was no evidence of lymphatic or vascular space invasion. Finally, the pathologist noted focal areas of stromal fibrosis and lymphocytic infiltration, findings that were suggestive of partial tumor regression. The final pathological diagnosis was: Conjunctival Malignant Melanoma, invasive to a depth of 1.8 mm, arising in the setting of Primary Acquired Melanosis with severe atypia. All surgical margins are negative for malignancy. Based on the AJCC 8th Edition staging for conjunctival melanoma, the tumor was classified as pT2aN0M0.

The patient had an uneventful postoperative recovery (Table 4). At the one-week follow-up, he reported mild foreign body sensation but no pain or visual disturbance. His visual acuity remained 20/20. The conjunctiva showed mild chemosis and injection, but the surgical site was healing well with no signs of infection or residual tumor (Figure 2). By the two-month postoperative visit, the patient was completely asymptomatic. The conjunctiva had healed completely, leaving a faint scar, with no evidence of local recurrence or new pigmented lesions. Systemic review revealed no new symptoms, and clinical examination showed no regional lymphadenopathy. A long-term, multidisciplinary management plan was established, involving ophthalmology and oncology. The plan includes ophthalmic follow-up every 3 months for the first two years, then every 6 months for the subsequent three years, and annually thereafter, along with annual systemic screening for metastasis.

3. Discussion

This case report documents a rare but clinically significant occurrence of a conjunctival malignant melanoma (CMM), with a measured thickness of 1.8 mm, arising from long-standing primary acquired melanosis (PAM) in an 18-year-old male. The case is particularly noteworthy due to the patient's young age, a demographic in which CMM is exceptionally uncommon. This presentation challenges the clinical heuristic that pigmented conjunctival lesions in young individuals are almost invariably benign and underscores the universal importance of histopathological evaluation for any melanocytic lesion demonstrating dynamic change.[11]

The conjunctiva, like the skin, contains melanocytes within its basal epithelial layer, which serve as the cell of origin for melanoma. The pathophysiology of CMM is thought to be closely linked to ultraviolet (UV) radiation-induced

mutagenesis.[12] Chronic UV exposure, particularly UVB (290-320 nm) and UVA (320-400 nm), induces the formation of covalent bonds between adjacent pyrimidine bases in DNA, creating cyclobutane pyrimidine dimers (CPDs) and 6-4 photoproducts. If these DNA lesions are not repaired by the nucleotide excision repair (NER) system, they can lead to characteristic "UV signature" mutations (C>T or CC>TT transitions) during DNA replication. These mutations can accumulate in key oncogenes and tumor suppressor genes, driving malignant transformation.[13] The patient's history of extensive unprotected sun exposure is a crucial etiological factor that aligns perfectly with this established pathophysiological mechanism.

Table 4. Postoperative Course and Follow-up Plan

Recovery Trajectory and Long-Term Surveillance Strategy

PHASE	PARAMETER	FINDING / DETAIL
Immediate Postoperative (1-Week Follow-up)	Patient Symptoms	Mild foreign body sensation; no pain or visual changes reported.
	Visual Acuity	Stable at 20/20 in both eyes.
	Clinical Signs	Mild conjunctival chemosis and injection. Surgical site healing well. No signs of infection or residual tumor.
Short-Term Follow-up (2-Month Follow-up)	Patient Status	**Completely asymptomatic.**
	Ocular Examination	Conjunctiva completely healed with a faint scar. No evidence of local recurrence or new pigmented lesions.
	Systemic Review	No new symptoms reported.
	Regional Examination	No palpable regional lymphadenopathy.
Long-Term Management Plan	Ophthalmic Surveillance	• **Years 1-2:** Follow-up every 3 months. • **Years 3-5:** Follow-up every 6 months. • **Year 5 onwards:** Follow-up annually for life.
	Systemic Surveillance	Annual systemic screening for metastasis (includes physical exam, lymph node survey, and consideration for imaging as clinically indicated).
	Multidisciplinary Care	Continued collaborative care involving Ophthalmology and Medical Oncology teams.

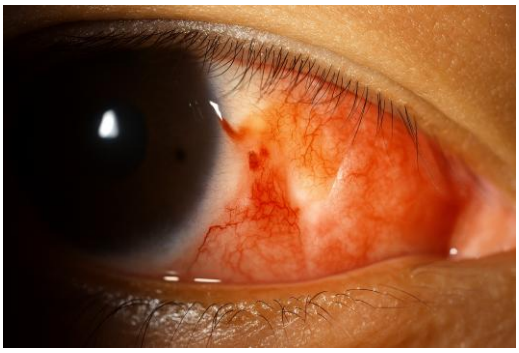

Figure 2. Postoperative clinical photograph of the patient's right eye two months after surgery. The image shows a well-healed conjunctiva with minimal scarring and no evidence of local tumor recurrence. The ocular surface is quiet and stable.

At the molecular level, CMM shares some genetic features with cutaneous melanoma but also possesses distinct characteristics. The mitogen-activated protein kinase (MAPK) pathway is frequently activated in CMM. Activating mutations in genes such as BRAF (most commonly the V600E mutation) are found in approximately 24-50% of cases, and mutations in *NRAS* are found in about 15-20%.[14] These mutations lead to constitutive activation of the MAPK signaling cascade, promoting uncontrolled cell proliferation and survival. Other recurrent mutations include those in the NF1 tumor suppressor gene and activating mutations in the TERT promoter, which lead to telomerase reactivation and cellular immortalization. The identification of these driver mutations has paved the way for targeted therapies (BRAF and MEK inhibitors) in the management of metastatic disease, making molecular profiling increasingly important.[15]

The histopathological confirmation that this patient's melanoma arose from PAM with severe atypia is consistent with the most common developmental pathway for CMM. PAM represents a spectrum of melanocytic proliferation within the conjunctival epithelium. PAM without atypia is a benign condition, whereas PAM with atypia is a true precursor to melanoma.[16] The diagnosis of atypia is made based on specific histopathological features of the melanocytes, including nuclear enlargement, hyperchromasia, irregular nuclear contours, prominent nucleoli, and epithelioid cell morphology.[17] As the severity of atypia increases, so does the risk of progression to invasive melanoma. The clinical challenge lies in that PAM often presents as a flat, brown, patchy area of pigmentation that can be difficult to distinguish from benign conditions like racial melanosis or a simple ephelis. However, any area of PAM that develops nodularity, increased thickness, vascularity, or extension onto the cornea, as seen in this patient, is highly suspicious for malignant transformation and warrants immediate biopsy.

The initial diagnosis of CMM is a clinical process, which is then definitively confirmed through histopathological analysis.[18] To guide their clinical assessment, clinicians often adapt the "ABCDE" mnemonic used for skin lesions. For the conjunctiva, this translates to A for age (higher risk in older patients), B for blood (the presence of prominent feeding vessels), C for color (variegation), D for diameter (larger lesions), and E for evolution (any documented change over time). This patient's lesion presented a compelling case for suspicion by exhibiting multiple of these warning signs. Most notably, it showed prominent feeder vessels (Blood), had variegated pigmentation (Color), and there was a clear, multi-year history of growth and darkening (Evolution). Furthermore, its location on the bulbar conjunctiva within the interpalpebral zone—the area most exposed to the elements between the eyelids—is the most common site for CMM, a fact strongly linked to maximal UV exposure.

Given these suspicious features, it was crucial to differentiate the lesion from a broad range of other pigmented conditions. The most common of these is a conjunctival nevus, a typically benign tumor that usually appears in the first two decades of life. While nevi can rarely transform into melanoma, they are often suggested by features like uniform pigmentation and the presence of clear, intrinsic epithelial cysts.[19] Another consideration is racial melanosis, which is common in darkly pigmented individuals and appears as bilateral, flat, patchy pigmentation in the perilimbal region and is not pre-malignant. A simpler lesion, the conjunctival ephelis or "freckle," is a flat, well-demarcated spot that does not progress to melanoma. Lastly, secondary pigmentation had to be ruled out, as discoloration can also arise from external causes like mascara deposits and foreign bodies, or from metabolic conditions such as ochronosis. The definitive distinction between these entities and melanoma requires histopathological examination, and a biopsy should never be delayed when malignant features are present. The management of this patient was based on established oncologic principles for CMM. The cornerstone of treatment is surgical excision. The use of a "no-touch" technique is paramount. This method minimizes manipulation of the tumor to prevent iatrogenic dissemination of malignant cells into the surgical field, circulation, or lymphatic system, which could lead to local recurrence or metastasis.

The decision to use 4 mm surgical margins is based on evidence showing that wider margins reduce the risk of local recurrence. While there is no universal consensus, margins of 2-4 mm are commonly advocated. The use of adjunctive cryotherapy is another critical component of modern management. Melanoma cells are sensitive to freezing temperatures. Applying double freeze-thaw cycles to the surgical bed and conjunctival edges effectively destroys any residual microscopic tumor cells that may extend beyond the visible lesion, significantly lowering the local recurrence rate, which historically has been as high as 50%. The decision not to use topical chemotherapy like Mitomycin C postoperatively was based on the achievement of clear surgical margins and the application of intraoperative cryotherapy, reserving chemotherapy for cases of diffuse PAM with atypia or recurrent disease. The prognosis of CMM is critically dependent on several histopathological factors. The most important is the Breslow tumor thickness.[20] Tumors thicker than 2 mm are associated with a significantly higher risk of metastasis and poorer survival. This patient's tumor thickness of 1.8 mm places him in an intermediate-risk category. While favorable compared to thicker tumors, it still carries a tangible risk of metastasis.

According to the AJCC 8th Edition staging for CMM, this patient is staged as pT2aN0M0. pT2a indicates a tumor of the bulbar conjunctiva with a thickness greater than 1.0 mm but not more than 2.0 mm, without ulceration. N0 means no clinical or radiological evidence of regional lymph node involvement and M0 means no evidence of distant metastasis. Other poor prognostic indicators include a non-bulbar location (forniceal, tarsal, or caruncular conjunctiva), ulceration, a high mitotic rate, and lymphovascular invasion. This patient's tumor had several favorable features: a bulbar location, absence of ulceration, and no lymphovascular invasion. The successful achievement of clear surgical margins is also a strong positive prognostic factor.

The occurrence of CMM in individuals under 20 is exceedingly rare. A review of the literature confirms that most cases are reported in patients over 50. When melanoma does occur in younger patients, it often raises questions about underlying genetic predispositions, such as familial atypical multiple mole melanoma (FAMMM) syndrome (associated with *CDKN2A* mutations) or xeroderma pigmentosum, though this patient had no such features. The clinical course and molecular profile of adolescent CMM are not well-defined due to the small number of reported cases. However, the fundamental principles of management—early detection, wide excision with adjuvant therapy, and long-term surveillance—remain the same. This case contributes valuable data to the

limited body of literature on CMM in this age group and serves as a potent reminder that oncologic principles should not be deferred based on age.

4. Conclusion

This case of an 18-year-old male with a 1.8 mm thick conjunctival malignant melanoma arising from primary acquired melanosis with atypia highlights several critical clinical tenets. It underscores that while CMM is rare in adolescents, it must be included in the differential diagnosis of any changing pigmented conjunctival lesion, irrespective of the patient's age. A detailed history focusing on lesion evolution and a meticulous clinical examination are key to early detection. The successful management of this patient, resulting in a disease-free status at two months, was predicated on prompt and aggressive intervention, combining wide "no-touch" surgical excision with essential adjunctive cryotherapy. The definitive histopathological analysis, including quantitative metrics like Breslow thickness, is indispensable for accurate staging, prognostic assessment, and guiding long-term surveillance. This case reinforces the necessity of a high index of suspicion and a multidisciplinary approach to optimize outcomes for this rare but potentially devastating ocular malignancy.

5. References

1. Cuffaro G, Fionda B, Piccinni F, Pagliara MM, Sammarco MG, Blasi MA, et al. Post-operative interventional radiotherapy (brachytherapy) in advanced ocular surface and eyelid tumors as an alternative to surgical retreatment. Eur J Ophthalmol. 2024; 34(4): 1266–76.
2. Weppelmann TA, Margo CE, Espana EM. Ocular surface fibroma: a rare, benign tumor of the conjunctiva. Ophthalmology. 2025; 132(2): e31.
3. Romeo MA, Taloni A, Borselli M, Di Maria A, Mancini A, Mollace V, et al. Iatrogenic ocular surface complications after surgery for ocular and adnexal tumors. Cancers (Basel). 2025; 17(9).
4. Queiroz de Paiva AR, Abreu de Azevedo Fraga L, Torres VLL. Surgical reconstruction of ocular surface tumors using fibrin sealant tissue adhesive. Ocul Oncol Pathol. 2016; 2(4): 207–11.
5. Julius P, Siyumbwa SN, Moonga P, Maate F, Kaile T, Kang G, et al. Clinical and pathologic presentation of primary ocular surface tumors among Zambians. Ocul Oncol Pathol. 2021; 7(2): 108–20.
6. Moon J, Choi SH, Lee MJ, Jo DH, Park UC, Yoon S-O, et al. Ocular surface complications of local anticancer drugs for treatment of ocular tumors. Ocul Surf. 2021; 19: 16–30.
7. Nguyen JQN, Drabarek W, Vaarwater J, Yavuzyigitoglu S, Verdijk RM, Paridaens D, et al. 8q gain has no additional predictive value in SF3B1MUT uveal melanoma but is predictive for a worse prognosis in patients with BAP1MUT uveal melanoma. Ophthalmol Sci. 2024; 4(2): 100413.
8. Jabbarli L, Biewald E, Guberina M, Rating P, Fiorentzis M, Flühs D, et al. Prognostic factors for surgical treatment of radiation-induced scleral necrosis after brachytherapy for uveal melanoma. Eur J Ophthalmol. 2025; 35(1): 357–66.
9. Chou H-D, Heimann H, Damato BE, Hussain RN. Inadvertent scleral perforation during choroidal melanoma surgeries: Incidence, risk factors, management, and outcomes. Am J Ophthalmol. 2025; 277: 356–64.
10. Huerva V, Vilardell F, Cid-Bertomeu P. Cryotherapy after topical interferon alpha 2b to treat conjunctival primary acquired melanosis. Case Rep Ophthalmol. 2023; 14(1): 111–4.
11. Svedberg K. Recurrence of primary acquired melanosis and conjunctival intraepithelial neoplasia. Ocul Oncol Pathol. 2023; 8(4–6):236–41.

12. Goemaere J, Lauwers N, de Keizer RO, Verdijk RM, de Keizer RJ. Bone metastasis in a case of primary acquired melanosis with atypia resulting from conjunctiva melanoma. Am J Ophthalmol Case Rep. 2023; 29(101730): 101730.
13. Oh AJ, Glasgow BJ. Dendritic melanocytic hyperplasia in Pterygia: a potential source of diagnostic confusion with primary acquired melanosis. Ocul Oncol Pathol. 2023; 9(1–2): 48–55.
14. Jin X, Zhang H. Spontaneous regression of primary acquired melanosis of the conjunctiva: a case report. Zhonghua Yan Ke Za Zhi. 2025; 61(6): 459–62.
15. Kanda M, Nghiem AZ, Shafi F, Hamed Azzam S, Gupta T, Daniel C. Primary acquired melanosis with spill over periocular lentigo maligna: 19-year outcomes at a specialist eyelid and ocular oncology centre. Br J Ophthalmol. 2025; 109(8): 909–16.
16. Andres T-S, Maria Jose V, Alexandro B. Acquired melanosis with hypertrichosis and intralesional acne in a 21-year old male patient: a treatment strategy. Health Prim Care. 2018; 2(4).
17. Mikkelsen LH, Andersen MK, Andreasen S, Larsen A-C, Tan Q, Toft PB, et al. Global microRNA profiling of metastatic conjunctival melanoma. Melanoma Res. 2019; 29(5): 465–73.
18. Kenawy N, Kalirai H, Sacco JJ, Lake SL, Heegaard S, Larsen A-C, et al. Conjunctival melanoma copy number alterations and correlation with mutation status, tumor features, and clinical outcome. Pigment Cell Melanoma Res. 2019; 32(4): 564–75.
19. Papaoikonomou MA, Pavlidis L, Apalla Z, Papas A. Conjunctival melanoma: a narrative review of current knowledge. Pigment Cell Melanoma Res. 2025; 38(2): e70006.
20. Esmaeli B, Ogden T, Nichols M, Lu T, Debnam JM, Dimitriou F, et al. Rate of response to immune checkpoint inhibitor therapy in patients with conjunctival melanoma. Melanoma Res. 2025; 35(2): 130–44.