When narrative medicine helps in the diagnosis of conjunctival melanoma – an exceptional case report

Abstract

Introduction: Conjunctival melanoma is a relatively rare ocular malignancy with substantial associated morbidity and mortality. It can arise in previously unblemished and unpigmented regions (approximately 10% of cases), from a preexisting nevus (approximately 20% of cases), or from the flat, spreading pigmentation of primary acquired melanosis with atypia (60–70% of cases), actually called conjunctival melanocytic intraepithelial neoplasia (C-MIN) with atypia (histopathologically more accurately term).
Purpose: The authors describe an extremely rare case of malignant conjunctival melanoma, with a long evolution, in a young black woman.
Results: Until now the patient has not shown any sign of relapse of this melanoma, after local excision.
Conclusion: Conjunctival melanoma is a condition of concern because of its rarity and lethal potential. Advances in the understanding and management of this neoplasm have markedly reduced the mortality and possibly the morbidity associated with this malignancy. We observe that there are some cases of conjunctival melanoma that might be cured with only a local excision with posterior cryotherapy without more aggressive methods. The practice of narrative medicine brings new possibilities in the diagnosis and collection of classical history.

Keywords: conjunctival melanoma, narrative medicine, treatment, oncology

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Introduction

Conjunctival melanoma is a rare condition, which occurs 40 times less than in the choroidal melanoma, and approximately 500 times less than cutaneous melanoma. Its incidence varies from 0.2 to 0.8/million in Caucasian population [1], [2], [3], [4]. It is usually identified in the conjunctiva perilimbal interpalpebral, but may arise in the eyelid, lower fornix, caruncle with worse survival prognosis in these areas [5]. This tumor appears in both sexes, without preference, arising predominantly from the 5th decade of life, particularly in Caucasians and is rare in black people. Recent studies indicate that as in the cutaneous melanoma, the incidence of conjunctival melanoma has been increasing [6], [7].
The natural history is not perfectly well established. They may appear as simple pigmented nodules which never suffer recurrence after local excision, or be more aggressive and may relapse.
This tumor results from the conversion of melanocytes and nevi. It can be pigmented or unpigmented performing in three clinical forms [8], [9], [10]:

1. **Hypermelanosis or conjunctival melanocytic intraepithelial neoplasia (C-MIN) with atypia (conjunctival in situ melanoma)** – about 50% of conjunctival melanomas: the tumor results from the evolution of a hipermelanosis with a prolonged and variable course. The primary suspected malignancy lies in the sudden appearance of one or more nodes in other planes of the lesion, which may or may not reach the surrounding skin;
2. **Primary melanoma without previous hypermelanosis**;
3. **Melanoma-derived pre-existing nevus**, which is very rare.

Local recurrence is common, with some studies reporting rates exceeding 50% [11]. Tumors can spread to regional lymph nodes and metastasize systemically [12].
The overall mortality rate is around 25% [13]. Tumors arising from the bulbar conjunctiva have a generally good prognosis with a survival of 5 years in about 100%. The survival rate of 5 years for tumors originating from the limbus is 80% and those originating in the palpebral conjunctiva is 50%. The poor prognosis in the latter case is explained by the delay in the diagnosis, because of its localization.

Case presentation

We report a case of a previously healthy 38-year-old black woman who presented herself to the Ophthalmology Department office for a routine evaluation, claiming to have

a lesion in the conjunctiva of the right eye (RE) with 5 years of evolution.

The patient presented a visual acuity of 10/10 in both eyes and the anterior segment showed on RE nasal pterygia grade II; on the left eye (LE) evidenced a pigmented lesion on the bulbar conjunctiva between the caruncle and the sclero-corneal limbus, slightly elevated with mild vascular tone and very pigmented, with a well-defined and fusiform appearance in the vertical and linear, sessile, which moved freely over the sclera (Figure 1). The same eye recognizes a pigmented lesion in the upper bulbar conjunctiva extending to the limbus esclerocornea located in the temporal area without accompanying nodules or abnormal vascularization (Figure 2, Figure 3).

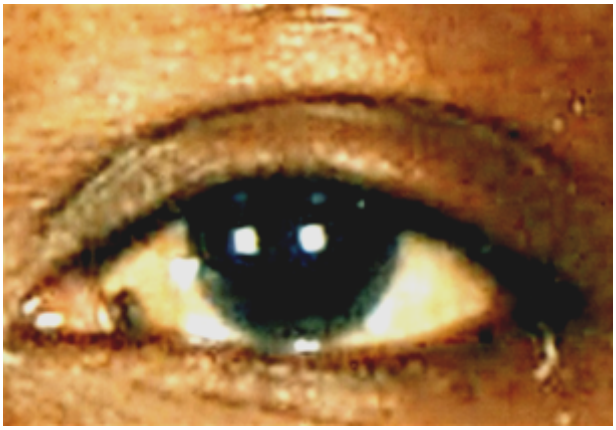

Figure 1: Clinical appearance of the lesion at first visit (LE)

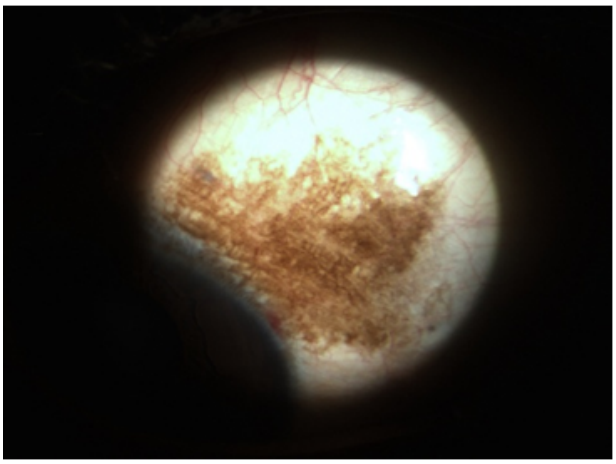

Figure 2: Clinical appearance of the temporal lesion at bulbar conjunctiva (LE)

Pupillary reflexes were present and symmetrical. The intraocular pressure was 13 mmHg in both eyes and the fundoscopy was normal.

It was scheduled pterygia surgery of the right eye.

In preparation for surgery the patient stated that for esthetic reasons she would like to excise the pigmented lesion in the left eye, which had become evident in recent months. The procedure was extended to the excision of the pigmented lesion of the left eye located in the nasal bulbar conjunctiva with a safety margin of 1 mm, with posterior histological analysis of the conjunctiva.

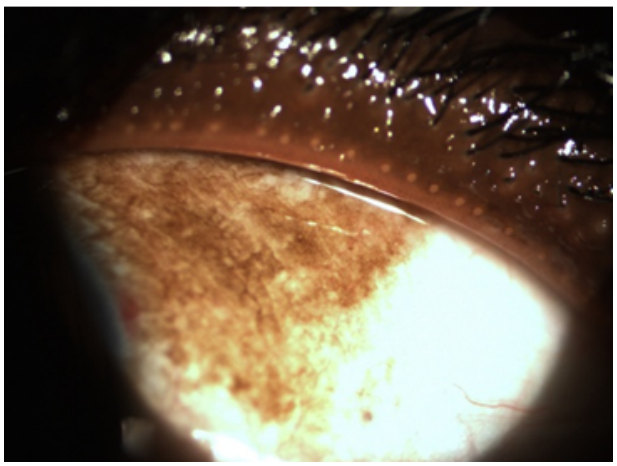

Figure 3: Clinical appearance of the temporal lesion at bulbar conjunctiva (LE)

At the time cryotherapy was not done immediately because it was thought as a first assumption that this was a nevus, since it had existed for several years.

Histopathologic examination of the specimen was made: Macroscopic findings: Elongated fragment with 0.8x0.6 cm with less than 1 mm of thickness, dark in color.

Microscopic findings: The excisional biopsy shows a neoplasic lesion composed of atypical cells with large vesicular nuclei and prominent eosinophilic nucleoli; the cytoplasm is clear or containing melanin; the neoplastic cells invaded superficial layers of the epithelium of the conjunctiva and, immunohistochemically, were reactive for Melan A and HMB-45, indicating cells of melanocytic origin. These features establishes the diagnosis of conjunctival melanoma (Figure 4, Figure 5).

It was asked to review the blade that confirmed the diagnosis, but it did not guarantee the safety margin at all operative part.

In the postoperative assessment and clinical follow-up, according to the protocol of our service, metastasis were not detected as shown by the tests used in the control protocol of these situations which include: chest x-ray, CT scan skull-brain and orbits, the analytical evidence liver function and liver ultrasound (search for hepatic and pulmonary metastasis), which are all within normal limits. The patient was examined by the specialties of dermatology and otorhinolaryngology for the detection of similar lesions and disseminated disease (mostly lymph nodes), the result was negative.

The patient also did a neck echography for detection of regional lymph node metastasis. We did not sentinel lymph node biopsy because it did not appear to have significant impact on survival or subsequent treatment [14]. Some studies referred patients who died of systemic metastasis had overt regional nodal involvement, which undermines the scope of sentinel node biopsy [13].

Fifteen days after the intervention, and with the knowledge of the histological results, we applied cryotherapy in the previous injury and in the edges of the entire injured area, in order to render inactive any melanocytes present in the waste bed of the same, and devitalize melanocytes that could eventually develop into melanoma recurrence.

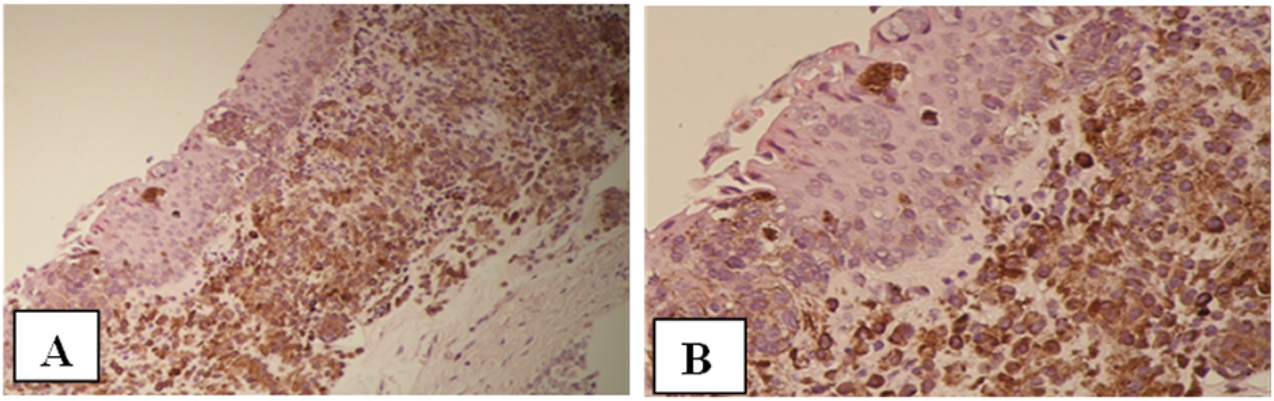

Figure 4: Fragment of lesion where it's possible to recognize pigmented tumoral mass (A). Higher magnification of the image preceding: the superficial layers of the epithelium of the conjunctiva are infiltrated by atypical melanocytes (B).

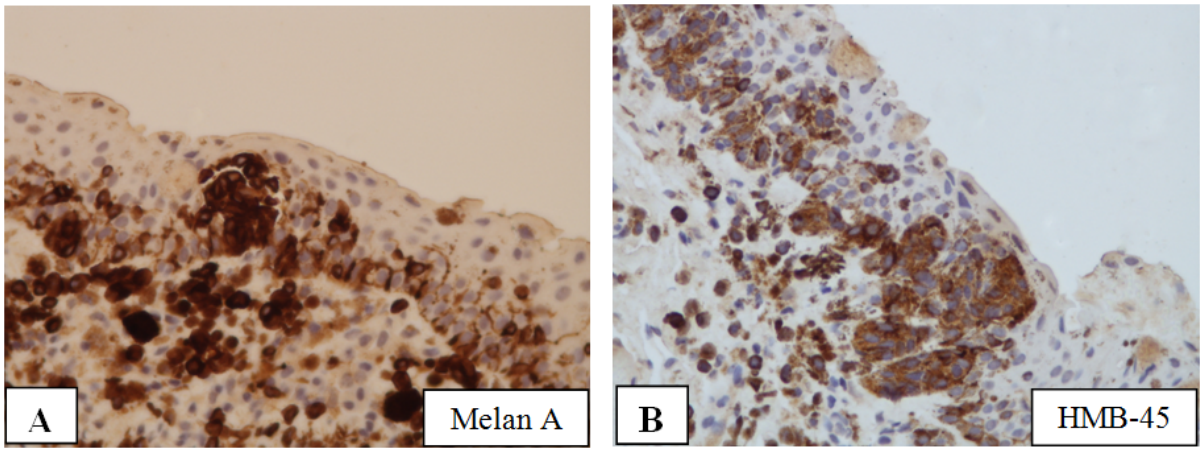

Figure 5: Immunohistochemical staining revealing that neoplastic cells were positive for melan A (A) and HMB-45 (B), indicating cells of melanocytic origin.

Clinical improvement after treatment was performed with Mitomycin C adjuvant topical 0.04%, 1 drop 4 times daily for a total of 7 days, in order to inactivate any residual melanocytes [15].
Currently, the patient is well without any evidence of lesions suggestive of metastasis in business, making a follow-up initially every 3 months.

Results

To date the patient does not show evidence of recurrence of the disease (Figure 6, Figure 7, Figure 8).

Discussion

Melanomas of the conjunctiva may arise anywhere in the conjunctiva.
Its classification according to the seventh edition of Tumor Nodes Metastasis (TNM system) from American Joint Committee on Cancer (AJCC) [16]:

A primary tumor (T) is classified as follows:

- TX – Primary tumor cannot be assessed
- T0 – No evidence of primary tumor
- Tis – Melanoma in situ
- T1 – Melanoma with 1.00 mm or less in thickness
- T2 – Melanoma 1.01–2.00 mm
- T3 – Melanoma 2.01–4.00 mm
- T4 – Melanoma with more than 4.00 mm in thickness

We can also subcategorize T classification in Ta (without ulceration and mitosis $<1/mm^2$) and Tb (with ulceration and mitosis $\geq 1/mm^2$).

Regional lymph nodes (N) are classified as follows:

- NX– Regional lymph nodes cannot be assessed (e.g. previously removed for another reason)
- N0 – No regional metastasis detected
- N1–3 – Regional metastasis based upon the number of metastasis nodes and presence of absence of intralymphatic metastasis (in transit or satellite metastasis)

We can also subcategorize N classification in Na (with micrometastasis) or Nb (with macrometastasis).

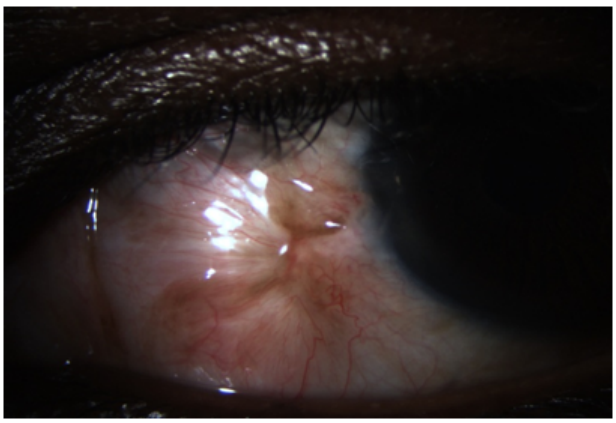

Figure 6: Appearence of the wound bed (LE)

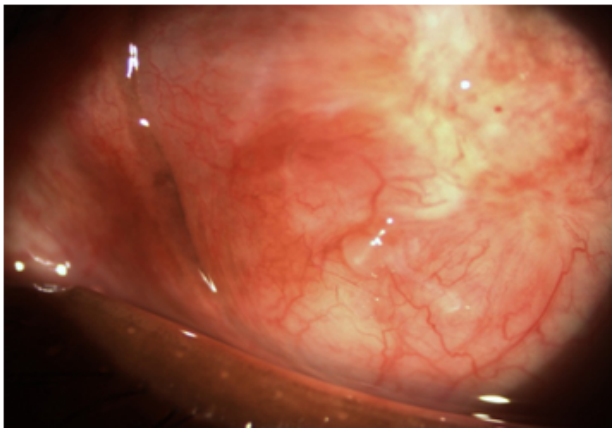

Figure 7: Appearance of the wound bed after cryotherapy and mitomycin C (LE)

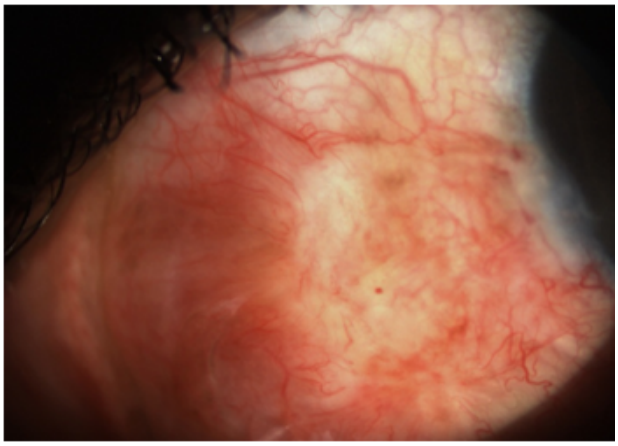

Figure 8: Appearance of the wound bed after cryotherapy and mitomycin C (LE)

Distant metastasis (M) is classified as follows:

- M0 – No detectable evidence of distant metastasis
- M1a – Metastasis to skin, subcutaneous or distant limph nodes
- M1b – Metastasis to lung
- M1c – Metastasis to all other visceral sites or distant metastasis to any site combined with elevated serum LDH

The treatment should be total excision as soon as possible after diagnosis, if possible with adjunctive cryotherapy in the wound bed and on the edges of the peri-lesional tissue [17].

Its spread is made by the lymphatics, affecting first the pre-auricular lymph nodes, and then the sub-maxillary and cervical [18], [19].

Predictive factors of metastasis included tumor origin de novo, palpebral location, nodular tumor, orbital invasion, diffuse intra-epithelial disease, local tumor recurrence, multifocal tumors, increased tumor thickness, high mitotic rate, epithelioid cells and lymphatic spread [9], [20], [21].

Predictive factors of death included tumor origin de novo, fornix location and nodular tumor [22].

Tumors in unfavorable locations, that is, those involving the palpebral conjunctiva, fornices, plica, caruncle, and lid margins, were associated with 2.2 higher mortality compared with (epi)bulbar melanomas [5].

Not all conjunctival melanomas are pigmented; melanomas with little or no pigment (amelanotic melanoma) can look like squamous and sebaceous gland carcinomas, papillomas, lymphoid hyperplasia, and even pterygia. Staining with the S-100 and Melan A protein stain and the more specific homatropine methylbromide (HMB-45) antibody stain can assist in diagnosis.

In the treatment, various techniques are resorted to, according to the variability of the prognosis. We must be cautious against incisional biopsy of possible conjunctival melanomas and encourage no-touch, en-bloc tumor excision, preserving natural barriers, using fresh instruments for conjunctival closure, adjuntive brachytherapy for deep invasion, and topical chemotherapy for intra-epithelial neoplasia [9]. There is still no consensus on dosage and duration of treatment with mitomycin, further studies are needed to establish the therapeutic protocol.

In our case, since the existence of conjunctival melanoma in black young adult persons is very rare [23], our initial investigation did not address screening for this clinical entity. In the context of pterygia surgery on the contralateral eye, we were confronted with this lesion in the left eye, and the patient requested excision for esthetic reasons.

However, based on the strengths of narrative medicine [20], a complementary strand of medicine based on evidence, while already in preparation for the intervention we chose the histological analysis of the piece that was excised in its entirety with wider margins.

If the benign lesions are treated as malignant they can lead the patient to unnecessary and agressive treatment, and on the contrary if malign lesions are not diagnosed we can be increasing the mortality rate if the treatment is not applied at an early stage. This case calls our attention to the need of a protocol to be followed in the case of conjunctival melanocyt lesions.

In fact there are few cases reported in the literature of conjunctival melanoma in young black adults (36 cases to date) [23]. This case is associated with these series.

The attitudes that were taken and the clinical outcome of the case after treatment were those that seemed more appropriate.

The present case is particularly interesting for showing the importance of histopathological examination of surgical pieces and fragments removed, even in lesions whose malignancy was deemed unlikely. We must emphasize the importance of narrative medicine in this clinical case, which was an essential tool for obtaining the diagnosis and consequent early treatment.
The anatomy and pathology study is essential where the clinic is justified or narrative description of the patient suggested.

Conclusions

The conjunctival melanomas are rare tumors, but their timely diagnosis is essential because of their high lethal potential.
The clinical history is very important and any change in the prior injury should be valued even if the patient appears to indicate irrelevant or no signs suggestive of malignancy.
It is therefore essential to recognize the growing size of nevi or atypical in the early stages of precursor lesions, namely MIN-C with atypia [8]. The staging of the disease by sentinel node biopsy is currently the first line of conduct in some centers [2], [13].
Surgical adjuvant cryotherapy is usually effective in eradicating most of the lesions. In the case of MIN-C with atypia topically cycles of mitomycin C can be applied 7 to 28 days, being a primary tumor treatment or adjuvant to surgery [15].
A biopsy of these lesions if there is a suspicion should be made using the technique “no touch” before a more aggressive approach is done. Its realization does not increase mortality, can be curative in certain situations and instead prevents mutilating and unnecessary surgeries.
The practice of narrative medicine brings new possibilities in the diagnosis and collection of classical history [24].

Notes

Competing interests

The authors declare that they have no competing interests.

Informed consent

The patient mentioned in the study gave his informed consent prior to the inclusion in the study.

Presentation at congress

The paper was presented at Clinical Reunion of Ophthalmology Department, Santa Maria Hospital, Lisbon (Portugal).

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