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Source / Izvornik: **Collegium Antropologicum, 2014, 38, 1187 - 1190**

Journal article, Published version

Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

Permanent link / Trajna poveznica: <https://urn.nsk.hr/urn:nbn:hr:105:722834>

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Download date / Datum preuzimanja: **2024-05-15**



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# Progression of Conjunctival Primary Acquired Melanosis (PAM) to Widely Spreaded Malignant Melanoma

Sonja Jandroković, Smiljka Popović-Suić, Jelena Juri Mandić, Tomislav Kuzman, Ivan Škegro, Marija Barišić Kutija, Sanja Masnec and Miro Kalauz

Department of Ophthalmology, University Hospital Center Zagreb, Zagreb, Croatia

## ABSTRACT

*Primary acquired melanosis (PAM) is an acquired pigmentation of the conjunctival epithelium, a preinvasive pigmented lesion. When it is associated with cellular atypia it can lead to the development of melanoma. We report a case report of malignant melanoma of the conjunctiva, which arrived from the conjunctival PAM. The disease was too extensive for ocular conservation, therefore exenteration was performed. This case highlights the need for regular follow-up of patients with melanocytic lesions of the ocular adnexa, and particular attention to the surgical technique, and careful follow-up to detect further disease activity.*

**Key words:** conjunctival malignant melanoma, primary acquired melanosis, local extension, orbital exenteration

## Introduction

Primary acquired melanosis (PAM) is an uncommon, almost always unilateral condition. It is characterized by proliferation of conjunctival epithelial melanocytes and it is not just deposition of pigment. The signs of PAM are irregular, unifocal or multifocal areas of flat brown pigmentation which may involve any part of the conjunctiva<sup>1</sup>. Primary acquired melanosis (PAM) is an acquired pigmentation of the conjunctival epithelium, a preinvasive pigmented lesion<sup>2</sup>. The other melanocytic lesions of the ocular adnexa include nevi and malignant melanoma<sup>2</sup>.

PAM can be with or without atypia. PAM with atypia is a pre-malignant condition. Most types of acquired melanosis remain benign, but if PAM is associated with cellular atypia, it can progress to conjunctival melanoma, according to some studies in up to 46% cases<sup>3</sup>. Malignant transformation should be suspected when a lesion shows nodularity, enlargement, or increased vascularity.

All suspicious lesions should be histological examined. Small areas of PAM can be observed and biopsy delayed unless they progress. However, pigmented lesions located on the palpebral or forniceal conjunctiva, plica or caruncle should increase clinical suspicion and lead to biopsy<sup>3</sup>. Although conjunctival melanoma has rare prevalence, it is potentially lethal ocular tumor.

This paper describes a report of one patient with conjunctival melanoma widely spreaded on the bulbar, tarsal conjunctiva and connection of the tarsal conjunctiva and eyelid skin. A discussion of the diagnostic and therapeutic considerations will follow.

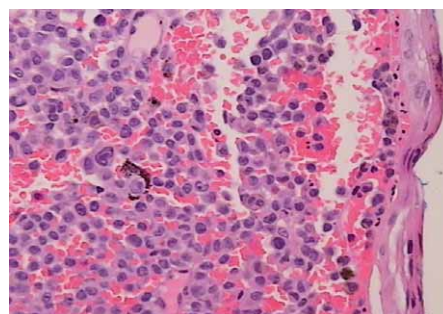
## Case report

A 69-year-old female patient was referred to our hospital with a pigmented lesion widely spreaded on the bulbar, tarsal conjunctiva and connection of the tarsal conjunctiva and eyelid skin of the right eye. The small pigmented lesion was reported 10 years ago after she has suffered a shot to the eye. In that time it was small, flat lesion next to the limbus. In her medical record it was reported as conjunctival melanosis. She was re-examined two more times in next 6 months. She did not refer to an ophthalmologist for many years, despite the recommended control examinations at least once a year.

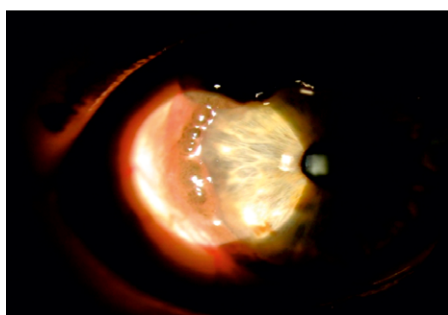
In December 2011 full ophthalmologic examination was performed and revealed nodular, large pigmented conjunctival lesion with increased vascularization and spreading on palpebral skin (Figures 1–3). There was no pigmented lesion on the left eye, but she had a record of



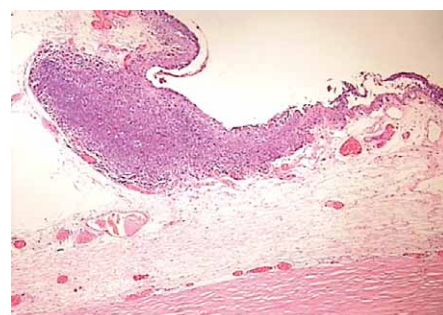
*Fig. 1. Conjunctival malignant melanoma of the right eye on first presentation with extension into the cornea, bulbar, forniceal and palpebral conjunctiva.*



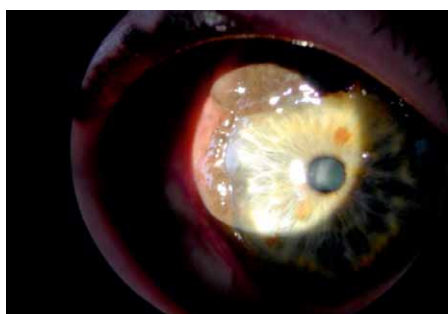
*Fig. 4. Conjunctival clip, partially ulcerated; tumor tissue composed of atypical melanocytes, some of which contain melanin pigment.*



*Fig. 2. Raised pigmented, nodular limbal lesion.*



*Fig. 5. Under conjunctiva and into the conjunctiva observes the melanoma tumor tissue.*



*Fig. 3. Extension of the malignant melanoma into the cornea.*



*Fig. 6. Melanoma tumor infiltrating subepithelial cornea, and stratified epithelium of the stroma (40x).*

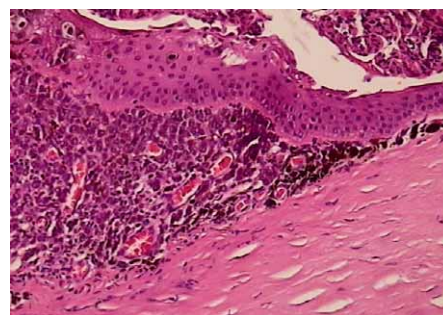
occlusion of the central retinal artery and cataract formation. Visual acuity on the right eye with correction was 0.7, and on the left eye was 0.3. Her affected eye was the eye with better visual acuity.

Conjunctival biopsy showed a tumor tissue composed of a cluster of atypical melanocytes whose nuclei contain prominent nucleoli compatible with malignant melanoma of the conjunctiva (Figures 4–7).

Ultrasound of the both eyes was within normal findings because the tumor was in front and was not available to the ultrasound analysis.

Magnetic resonance imaging (MRI) revealed no spreading to the orbita.

Before therapeutic decision, MSCT (brain, orbital, abdomen, thorax, sacrum) was performed for melanoma staging. There was no evidence of metastatic disease.



*Fig. 7. Melanoma tumor infiltrating subepithelial cornea, and stratified epithelium of the stroma (200x).*

On skeletal scintigraphy (Tc-99m MDP) there was no evidence of the pathologic accumulation.

As the oncologist said that with primary irradiation it is not possible to achieve a longer control of the disease, the only therapeutic approach was radical surgery.

The disease was too extensive for ocular conservation. With an informed written consent she was presented for surgery. Exenteration of the right orbit was performed. Postoperative recovery was uneventful. Psychiatrist was consulted and he recommended therapy.

A month later, she underwent a cataract surgery on the left eye with slightly better visual result. The patient has participated in regular follow up. PET-CT scan was performed once a year. There were no further problems for more than two years to date.

We report a case of malignant melanoma of the conjunctiva with local spreading on a bulbar, tarsal conjunctiva and connection of the tarsal conjunctiva and eyelid skin. There was no evidence of distant metastasis.

## Discussion

PAM of the conjunctiva has been the subject of controversy in incidence, natural course and management<sup>4–7</sup>. PAM accounted for 11% of all conjunctival tumors and 21% of melanocytic lesions<sup>5</sup>. The best clinical approach is still a matter of debate.

Pigmented lesions of the conjunctiva may be melanocytic or non-melanocytic. Melanocytic lesions of the conjunctiva can be classified into nevi, melanosis and malignant melanoma<sup>8</sup>. Conjunctival nevus is the most common melanocytic lesion of the conjunctiva. They can vary in size and pigmentation. They are usually mobile over the surface of the globe<sup>9</sup>.

PAM of the conjunctiva is acquired, almost always unilateral, brown or tan colored flat lesion of the conjunctiva. It affects mainly adults, with median age at referral 56 years<sup>4</sup>. PAM is classified on the basis of histopathology into PAM without atypia and PAM with atypia.

It differs from a nevus historically as it is acquired in middle age, and clinically lacks a cystic component<sup>9</sup>.

Architectural abnormalities and cytological features are criteria for defining atypia.

Discontinuous lentiginous spread of atypical melanocytes, extension above the basal layer of the epithelium with intraepithelial nesting, full thickness epithelial disposition and pagetoid ascent are the most important architectural abnormalities. Cytological changes are nuclear hyperchromasia and enlargement, epithelioid morphology. Also there should be immunohistochemical evidence of the melanocytic proliferation and increased cell proliferation<sup>9</sup>.

PAM with severe atypia shows progression to melanoma in 13%<sup>2</sup>.

Malignant melanomas of the conjunctiva are rare but potentially lethal. They are accounting for less than 2% of ocular malignancies<sup>9–11</sup>. Malignant melanoma of the conjunctiva can arise from apparently normal conjunctiva, from PAM and from naevi<sup>12</sup>.

The tumor can spread through lymphatic and bloodstream. It most commonly metastasizes to the lung, liver, brain and bone. Also it can directly extend to the globe and orbit<sup>13</sup>. Limbal location may carry greater risk of intraocular spread<sup>10</sup>.

While the management of PAM depends on the extent of involvement, the management of the conjunctival melanomas includes surgical resection with a wide margin excision<sup>9,14</sup>.

PAM can be just observed, but in suspicious cases excisional biopsy is mandatory.

Surgical resection of the malignant melanoma of the conjunctiva must be planed like wide surgical excision with a wide margin excision (more than 3 mm)<sup>13,14</sup>. Also

Cryotherapy may be included, topical mitomycin C(MMC) and/or alcohol epitheliectomy<sup>9</sup>, and topical interferon  $\alpha$ -2b<sup>15</sup>. Also radiotherapy can be a method of choice in some cases, such as orbital recurrences.

As malignant melanoma can metastasize, it is very important to examine the patient's regional lymph nodes, and consult the oncology service for a systemic metastatic workup<sup>9</sup>.

For the evaluation of cutaneous melanoma PET-CT has a large value. Sensitivity and specificity for detecting metastasis are higher for PET than for any other conventional imaging procedures<sup>16</sup>.

PAT-CT can detect lymph node metastasis and guide initial staging of patients with conjunctival melanoma<sup>17</sup>.

As the malignant melanoma of the conjunctiva is rare, there are some difficulties with staging. For a correct diagnosis, decision of treatment procedure and patients follow-up is very important to have good multidisciplinary approach.

This case emphasizes the need for some important rules in case of pigmented conjunctival lesions:

- Regular observation of a small PAM lesions (<3 clock hours).
- Performing an excisional biopsy for a larger lesion.
- All suspicious lesions should be histologically examined.
- Appropriate surgical resection of malignant melanoma of the conjunctiva and implementing the other therapeutic procedures if needed.
- Good examination of the patient for a possible metastasis.
- Long follow-up of the patient with appropriate imaging procedures.

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*S. Jandroković*

*Department of Ophthalmology, University Hospital Center Zagreb, Kišpatićeva 12, 10 000 Zagreb, Croatia  
e-mail: sonja.jandrokovic@gmail.com*

## PROGRESIJA PRIMARNE MELANOZE SPOJNICE U RASPROSTRANJENI MALIGNI MELANOM SPOJNICE

### SAŽETAK

Primarna melanoza spojnice je stečena pigmentacija epitela spojnice, preinvazivna pigmentna lezija. Kada se razvije stanična atipija može nastati melanom. Prikazujemo slučaj malignog melanoma spojnice koji se razvio od primarne melanoze spojnice. Bolest je bila izrazito rasprostranjena, oko se nije moglo sačuvati i u svrhu liječenja je učinjena egzen-teracija orbite. Ovim prikazom slučaja želimo istaknuti važnost redovitih kontrola pigmentnih lezija spojnice i očnih adneksa. Iznimno je važno obratiti pozornost na planiranje kirurške tehnike te nastaviti praćenje aktivnosti bolesti redovitim kontrolama.