Management of primary acquired melanosis (PAM) of the eye *(State of Research Paper)*

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Abstract

With regard to acquired melanosis of the conjunctiva, there is still neither a worldwide uniform nomenclature nor reliable data on how frequent this type of pigment disorder is. This is even more true for the estimation of the risk of progression into cancer as well as the clinical management of this entity. This short paper presents the current, partly contradictory knowledge which is available.

Findings and Discussion

While melanosis of the body skin is generally an entity harmless in nature, melanosis of the eye is a serious finding. It is the term used for patchy, blotchy, and ill-defined pigmentation of the anterior segment of the eye that cannot be assigned to other entities such as nevi. Their pigmentation varies widely from colorless to dark brown. Depending on the type and localization, a distinction is made between congenital, ethnic and other (primary) melanoses and acquired melanoses. In addition, pigmentation of the anterior segment of the eye also occurs with substance deposition (e.g., certain drugs) and after inflammation (postinflammatory hyperpigmentation).[1-3] So-called ethnic melanoses occur almost regularly in people of dark skin type, usually bilaterally (on both eyes), sometimes symmetrically. Acquired melanoses, on the other hand, tend to affect fair-skinned, middle-aged people. However, the exact names and delimitations of the different melanoses of the eye have been redefined again and again in the past decades and until today there is no final, uniformly accepted classification. The only certainty is that congenital melanoses are considered to be low-risk (melanosis oculi) or completely harmless (ethnic melanoses) with regard to the potential for degeneration into cancerous lesions.

Regarding acquired melanoses (PAM), doctrinal opinions differ widely regarding frequency and degeneration risk. While some researchers consider the risk of degeneration of acquired melanoses to be up to 50%, others describe a prevalence of acquired melanoses of up to 36% of the population. With an incidence of approximately 1/1,000,000 per year for malignant melanoma of the anterior segment of the eye, this would imply a vanishingly small risk of cancerous transformation of acquired melanoses.[8-10] However, all figures published so far are extremely contradictory and do not give a clear picture at all. Therefore, the opinion of most researchers is to consider all acquired melanoses as generally risky until a conclusive research of this disease is done and it is recommended by ophthalmological societies to have them checked by an ophthalmologist at regular intervals. Changing, large, or otherwise suspicious findings are usually surgically removed, as melanoses with cellular atypia are thought to have a particularly high risk of degeneration. While some researchers consider the risk of degeneration of acquired melanoses to be up to 50%, others describe a prevalence of acquired melanoses of up to 36% of the population.[10,11]

With an incidence of approximately 1/1,000,000 per year for malignant melanoma of the anterior segment of the eye, this would imply a vanishingly small risk of degeneration of acquired melanoses as well. Melanosis oculi, in contrast, is a congenital hyperpigmentation of the medial eye skin (uvea or the lamina episcleralis), not of the conjunctiva. When skin pigmentation is observed in addition to pigmentation of the eye, this is referred to as nevus ota. Differentially, melanosis oculi must be distinguished from other, potentially more dangerous acquired PAM. Melanosis oculi has normally to be checked by an ophthalmologist due to a possible risk of transformation.[1,2]

Regarding PAM all figures published so far are extremely contradictory and do not give a clear picture at all. Therefore, the opinion of most researchers is to consider all acquired melanoses as generally risky until a conclusive research of this disease is done and it is recommended by ophthalmological societies to have them checked by an ophthalmologist at regular intervals. Changing, large, or otherwise suspicious findings are usually surgically removed because melanoses with cellular atypia are considered to have a particularly high risk of developing malignancy. However, PAMs are usually so widely "scattered" and often interspersed with colorless areas that complete surgical removal is impossible in many cases. Diagnosis and management of ocular melanoses is further complicated by the fact that to date there are no clear clinical criteria to distinguish congenital, ethnic and acquired melanoses, nor is it possible to differentiate non-melanocytic pigmentations of the eye in ophthalmologic examinations. A reliable differential diagnosis is only possible for specially trained pathologists.[12,13]

The terminology associated with PAM is controversial. The World Health Organization adopted the term primary acquired melanosis (PAM). Ackerman, a dermatopathologist, confused the medical community with the term "melanoma-in-situ of the eye" analogous to lentigo maligna of the skin. While the term melanoma-in-situ may apply to a few PAM with severe atypia, it is still useless because many PAM lesions have no tendency to develop into melanoma. We believe that the term melanoma-in-situ may unnecessarily cause unnecessary fears for both clinicians and patients; especially since many PAM lesions have little tendency to evolve into melanoma. This is especially true since Gloor and Alexandrakis determined the true incidence by screening all of their Caucasian patients older than ten years who were referred to an eye clinic for unrelated conditions. Using less rigorous criteria for diagnosis, they concluded that a PAM lesion was found in 36% of their patients. What is more, in some cases it may be difficult or even impossible to determine histopathologically whether low-grade melanocytic hyperplasia is present or whether conjunctival pigmentation reflects melanin pigment within squamous cells. Immunohistochemical staining for melanocytic and epithelial markers may help to make this distinction correctly in difficult cases.[14,15] On the other hand, the question of relevance arises because Shields et al. have elaborated that PAM without atypia and PAM with mild atypia virtually never progress into a melanoma.[10]

Our preliminary conclusion for the clinical management of PAM, based on the currently available scientific literature, is that all patients with PAM should have their lesions photographed in a clinic equipped with adequate ophthalmic cameras.

- If the melanotic portion of a PAM is confined to the bulbar conjunctiva and has an extension of less than 1 clock hour, we currently believe that follow-up examinations once or twice a year (with new photographs each time) are sufficient unless a well-informed patient specifically requests excision.[11]

- If a PAM has an extension of 1 to 2 clock hours, the patient should be counseled in detail, honestly admitting that medical science does not yet fully understand PAM, and offered the options of observation or excision (if this treatment is possible).
- If the lesion is larger than 2 clock hours, especially with macroscopic evidence of atypia, we believe surgical excision and cryotherapy should be considered (if this treatment is possible).[6,13-15]
- Large diffuse PAMs or those where amelanotic areas are suspected can be further diagnosed with small map biopsies.[12]
- If extensive conjunctival tissue must be removed and primary closure is difficult, amniotic membrane or buccal mucosa transplant must be used.[13,15] This fact alone should be considered a warning that any overtreatment of a PAM may also cause some harm to the patient. Biopsies of the conjunctiva are by no means the minor cuts we are familiar with in dermatology.
- Corneal PAM can be treated with either alc. epitheliectomy or topical mitomycin C.
- Depending on subsequent clinical and histopathologic findings, adjunctive treatment for residual or recurrent PAM may include in-office cryotherapy or topical chemotherapy.

Conclusion

In summary, PAM is far more common than previously thought. Knowledge of it among researchers and clinicians is still alarmingly low, considering that apparently up to 36% of the population has (small and mildly pigmented) unilateral conjunctival melanosis, and small PAMs (<1 clock hour) seem to remain stable. We also believe that PAMs without macroscopic atypia have only a minimal risk of progression to melanoma, whereas PAMs with macroscopic atypia may have a >10% risk of transformation to melanoma. Careful, precise, long-term follow-up is recommended for all patients with PAM.

Prospects

After reviewing the existing literature, we would not be surprised if PAM would one day be divided into two distinct entities. One that is simply a true melanosis, as harmless as anywhere else on the body, and another that is related to what we know in dermatology as lentigo maligna. Further research on this is urgently needed.

Conflicts of interest

None.

Ethical standards and patient's rights

This article is about scientific facts based on research literature. It is not reporting on a clinical trial, especially not a prospective one. Our research work is always conducted in accordance with the Declaration of Helsinki.

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