CLINICAL STUDY

Conjunctival nevus and melanoma

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Abstract

The conjunctival nevus is one of the most common benign tumors of the ocular surface. Melanomas are rare; they can arise without a preexisting conjunctival nevus, or due to malignant transformation in case of PAM (primary acquired melanosis). The retrospective study analyzed 70 patients with pigmented lesion of the conjunctiva in period 1996–2006 at the Department of Ophthalmology, Faculty of Medicine, Comenius University, Bratislava, with the aim to determine the frequency of change in size and pigmentation of these benign lesions. Epibulbar pigmented lesions are rare, recognition of their precursors lesions at an early stage is important. Surgical excision is usually effective in eradicating these lesions. Extensive cases of flat primary acquired melanosis with atypia may be managed with mitomycin C. Multifocal and advanced melanoma, especially showing intraocular or orbital invasion, may require exenteration and/or radiotherapy to adequately extirpate the neoplasm locally. However, systemic metastases might have already develop in patients with advanced stage of disease (Fig. 7, Ref. 13).

Key words: conjunctival nevus, epibulbar melanoma, primary acquired melanosis.

The predominant benign conjunctival melanocytic lesions are composed of a variety of nevi and melanosis that have a predilection for the perilimb bulbar conjunctiva. Nevi are believed to be congenital lesions that are generally unilateral. They are usually first identified in early adulthood, they frequently develop cysts and become slightly elevated and may change in color and size. Dark brown melanotic pigmentation is normally observed in the conjunctiva, a condition referred to a racial melanosis, which is evident bilaterally form an early age in more pigmented races. This condition is usually caused by an excess production of melanin or hyperpigmentation by the melanocytes (forming an ephelis) or benign proliferation of melanocytes (forming a benign lentigo).

The terminology associated with melanosis is controversial, especially when melanosis is unilateral and acquired, in that case lesion can be a precursor of invasive melanoma. Some authors referred this unilateral acquired pigmentation as a precancerous melanosis, which in the past has led to an inappropriate aggressive therapy - frequently exenteration of the orbit (surgical excision of the orbital contents - the eyeball, muscles, and eyelids, too.) As a result, others have referred these lesions as benign acquired melanosis, but this terminology has caused concern that the malignant potential of this condition may be overlooked.

Fig. 1. Histopathological findings in 70 cases of epibulbar pigmented lesions (Dept of Ophthalmology, Bratislava).

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Because these lesions may show variable histological findings, WHO proposed the term primary acquired melanosis (PAM) with or without atypia for these lesions.

Conjunctival melanoma is relatively rare condition, occurring only in 1/40th compared to choroidal melanoma and approximately 500 times less often than cutaneous melanoma. Its incidence is 0.2 to 0.8 per million in white population. Conjunctival melanoma is a potentially lethal neoplasm, with an average 10-year mortality rate of 30%. It is identified most frequently in the perilimbal interpalpebral bulbar conjunctiva with tumor masses located in the palpebral or fornical conjunctiva or caruncle, plica semilunaris or eyelid margins having a worse prognosis for sur-
vival. Conjunctival melanoma has no sexual predilection, and it is found predominantly in middle-aged adults. This disease occurs mainly in white population, with rare reports in black on other populations. Recent studies have indicated that the incidence of epibulbar melanoma is increasing similarly to cutaneous melanoma.

Conjunctival melanomas are malignant tumors of proliferating melanocytes that are derived from the neural crest. The conjunctiva is a mucous membrane covering the anterior half of the pericorneal globe (bulbar conjunctiva) and lining the posterior surface of the eyelids (palpebral conjunctiva) forming a fold in the superior and inferior fornices (forniceal conjunctiva). Since the conjunctival stroma (the substantia propria) contains blood vessels and lymphatic vessels, a malignancy that invades the sub-epithelial region has a potential for local and systemic metastases.

The aim of the treatment is to reduce the opportunity for spreading the tumor mass. Dissemination can be done by local extension and by spread into the regional lymphatic nodes (ipsilateral, preauricular and submandibular lymph nodes), which are the most common site for metastasis. The mortality rate is over 25%. When tumor arises from PAM, the mortality rate increases to 40%.

Other indicators of a poor prognosis are involvement of the palpebral conjunctiva, fornix conjunctiva or caruncle, severe cellular atypia, invasion into deeper ocular tissues, greater than 5 mitotic figures per high-power field, lack of an induced inflammatory response.

Material and methods

In the study, 70 cases of pigmented lesions of the ocular surface were analyzed. Included were 47 male (67.1%) and 23 female (32.9%) patients with the mean age 45 years (from 18 to 76 years). In the group of patients, all pigmented epibulbar lesions—brown, dark brown and semi-pigmented lesions were included. Unilateral lesions were observed in 64 cases (91.4%). In 68 (97.1%) cases, nevi or primary acquired melanosis of the conjunctiva was found, only in 1 case malignant epibulbar melanoma was histologically verified, and in 1 case epibulbar pigmented lesion-outgrowing through the sclera in case of verified intraocular choroidal melanoma after combined therapy (irradiation, endovitreal surgery) was observed. The most common locations of the nevus were the bulbar conjunctiva – 59 cases (84.3%), caruncle – 7 cases (10%) and plica semilunaris – 3 cases (4.3%). Verified case (4.3%) of melanoma arose primary from caruncle. Nevi were most commonly seen within the nasal and temporal portions of the bulbar conjunctiva. Intra-lesion cysts were present in 48 patients (69.6%) – clinically – by slit lamp examination. The indication for excision and histopathologic examination were changes in color (gradually darkened) and shape of the pigmented mass in patients, who returned for periodic observation (3 month interval). Primary indication for surgical intervention was localization of the nevus on the limb near to the cornea in patients, who wanted to correct their refractive error by contact lenses.
Fotka ktorého pacienta je vlastne na obrázku č.6? Pacienta narodeného 1954 alebo pacienta narodeného 1947?

**Results**

Histopathological findings after excision showed melanocytic nevocellular nevus in 52 cases (74.3 %), single nevus with atypia in 4 cases (5.7 %), without atypia in 3 cases (4.3 %), primary acquired melanosis in 10 cases (14.3 %) (Fig. 1–7).

In all examined lesions the margins and the bottom of the mass were free. In 30 cases (42.9 %), plastic surgery of the conjunctival sac was necessary.

The melanoma case (male, 48 years old) with verified melanoma arising primary from the caruncle came to our clinic in stage of disease T3 N0 M0, histologically the melanoma was confirmed, but he didn’t accept indicated radical surgery – exenteration of the orbit. After 6 months, the visit confirmed the tumor mass grow from the primary localization in caruncle to the space of upper and lower fornix, but without infiltration to the orbit. Other examinations (also PET) excluded metastases and the patient is monitored.

**Discussion**

The clinical features of pigmented lesions involving the conjunctiva can occasionally overlap. Most of previous reports have provided data on the histopathological features of conjunctival nevi. The frequency of nevi involving the tarsal or fornical conjunctiva may support the notion that pigmented lesions in these areas may not be nevi and that other conditions, such as conjunctival melanoma, should be considered. The majority of conjunctival nevi (over 60 %) in our study contained cysts, which are not seen in conjunctival melanoma.

Recognition of the melanoma precursors at an early stage is important. Staging of the disease by sentinel lymph node biopsy is now advocated in some centers. Surgical excision with adjuvant cryotherapy and alcohol corneal epithelialectomy is usually effective in eradicating most of these lesions. Extensive cases of flat primary acquired melanosis with atypia may be managed with mitomycin C. Multifocal and advanced melanoma, especially in cases showing intraocular or orbital invasion, may require exenteration and/or radiotherapy to adequately extirpate the neoplasm locally. However, systemic metastases may have already developed in patients with advanced disease.

Conjunctival melanoma is a serious condition due to its rarity and lethal potential. Approximately 75 % of these neoplasms arise in the area of PAM with atypia requiring histopathologic examination for the diagnosis. When thickening of conjunctiva is present in the area of PAM, the development of an invasive malignant melanoma should be considered.

It is important to provide an excision of all suspected lesions with “no touch technique”.

**References**


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