

Advances in Melanocytic Lesions of Conjunctiva

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Handout

Particularities of conjunctiva as compared to the skin

Conjunctival lamina propria is a thin layer of loosely collagenous tissue rich in vascular supply and in immediate contact to Tenon's capsule, sclera, ocular adnexae, and to anterior orbit. As a protective barrier conjunctival lamina propria is less efficient than dermis. Constant mechanical abrasion due to blinking favors development of flattened conjunctival lesions.

On the other hand translucency and large mobility of conjunctiva over the underlying tissues permits early detection of lesions and easier assessment of depth of location and attachment to deep structures. But palpebral and forniceal conjunctival location of melanocytic lesions are often time related to delayed diagnosis.

Lesions of the conjunctiva not derived from melanocytes that may simulate pigmented lesions

Pigmented squamous lesions (papillomas or conjunctival intraepithelial neoplasia with various degrees of dysplasia up to squamous cell carcinoma, including spindle cell carcinoma)

Pharmaceutical agents (epinephrine plaques, argyrosis, minocyclin deposits)

Metallic (foreign bodies, iron, heavy metals) or industrial products (quinones, aniline dyes) deposition

Mascara deposits

Lymphoid lesions ("salmon patch" lesions)

Mesenchymal proliferative conditions (fibroma, fibrous histiocytoma, elastofibroma, myxoma, nodular fasciitis)

Juvenile xanthogranuloma

Neurofibroma

Pinguecula and pterigium

Pyogenic granuloma

Hemangiopericytoma

Inflammatory conditions (sarcoidosis, other granulomatous or allergic processes)
Pseudopigmentations (blue sclera, staphyloma, scleromalacia perforans)
Endogenous pigmentations (hemosiderin, bilirubin depositions, Addison disease, Peutz-Jegher syndrome)
Metabolic disorders (ochronosis, Gaucher's disease)

Ephelis (freckle)

Increased local pigmentation in basal epithelial cells without melanocytic hyperplasia

Complexion-Associated conjunctival pigmentation (racial melanosis)

Increased bilateral and symmetrical pigmentation in basal epithelial cells without melanocytic hyperplasia is seen. The pigment tends to be most intense at the limbus, fanning out toward the fornices.

Lentigo simplex

Increased local pigmentation in basal epithelial cells with basal melanocytic hyperplasia

Nevi

Congenital or acquired hamartomatous, well circumscribed, melanocytic lesions on epibulbar conjunctiva, plica, caruncle, or eyelid margins: rarely seen on palpebral conjunctiva.

Specific to conjunctiva are Henle epithelial crypts entrapped in subepithelial nevi forming cystic spaces.

Generally follow the description of their skin counterparts:

- junctional nevi
- subepithelial nevi (analogous to intradermal nevi)
- compound nevi
- blue nevi
- dysplastic nevi (proliferation of cytologically atypical melanocytes attached to a nevus)
- Spitz nevi
- Congenital melanosis oculi and congenital oculodermal melanosis (nevus of Ota): defect of melanocyte migration with formation of diffuse blue nevus in skin, periocular soft tissues, episclera, and sclera in the distribution of the ophthalmic branch of trigeminal nerve; associated with melanocytic proliferation in uveal tract, meninges of optic nerve and orbital periosteum.

Primary acquired melanosis

Specific terminology is used by ophthalmologists and ophthalmic pathologists although the lesions match their skin counterparts. In an effort to reconcile different terms used in the past, the World Health Organization proposed the currently used term of Primary Acquired Melanosis (PAM) which better characterizes conjunctival melanocytic lesions where application of cutaneous criteria of asymmetry, superficial spreading, and depth of invasion are problematic.

Clinically it presents as an acquired unilateral golden-brown flat pigmentation of the bulbar, forniceal, or palpebral conjunctiva in middle aged persons. It displays irregular borders, variable degrees of pigmentation, relentless growth, or “waxing and waning” evolution. Palpebral lesions are sometime continuous with lentigo maligna (Hutchinson freckle) of the eyelid skin. Characteristically PAM is freely movable over sclera.

PAM without atypia (31% of cases)

Some show basal conjunctival epithelial hyperpigmentation without melanocytic hyperplasia (reactive acquired melanosis). Histomorphologic overlap with freckle, but clinically more widely spread.

Some show conjunctival epithelial hyperpigmentation with melanocytic hyperplasia which is uniform and confined to basal layer. Histomorphologic overlap with lentigo simplex but clinically more widely spread.

Both have extremely low potential to evolve to melanoma.

PAM with atypia (68% of cases)

Conjunctival melanocytes harbor enlarged nuclei, palisading of enlarged melanocytes along the basal layer, local pagetoid invasion of melanocytes into the conjunctival epithelium, and nesting of melanocytes. Lesional melanocytes are characterized by cytologic and architectural features which are used to classify PAM with atypia into low and high risk categories for invasive melanoma. The skin counterparts of these two entities could be considered lentigo maligna and lentigo maligna melanoma, respectively. Low risk cytologic atypia includes small polyhedral, spindle, and large melanocytes with pigmented arborizing dendrites. High risk cytologic atypia includes epithelioid melanocytes (75% risk of evolution to malignant melanoma).

Low risk architectural growth patterns are basilar hyperplasia, basilar nesting, and occasional suprabasilar intraepithelial nesting (all 22% risk of evolution to malignant melanoma). High risk architectural patterns are pagetoid involvement (multiple “buckshot” type melanocytic clusters of various sizes) and nearly complete epithelial replacement (both 90% risk of evolution to malignant melanoma).

Malignant melanoma

Invasion of conjunctival lamina propria and neighboring structures by atypical melanocytes is the harbinger of conjunctival malignant melanoma. In 35-40% of cases malignant melanomas arise from junctional (rare) or compound nevi; in 25-30% of cases they come from primary acquired melanosis; and in 25-30 of cases they arise de novo or

indeterminately. The ones arising from preexisting nevi have a slightly better prognosis than the ones arising in preexisting PAM with atypia or arising de novo. Melanomas in this location can be primary or secondary (from intraocular or distant skin melanomas).

Prognostically important factors are:

- unfavorable locations: palpebral conjunctiva, fornices, plica, caruncle, and lid margins
- favorable location: bulbar conjunctiva
- depth of invasion (measured from the epithelial surface): less than 1.5 mm the prognosis for life is excellent
- some studies consider this threshold at 0.8 mm and consider lesions of 1-4 mm to have a two times higher death rate while those of greater than 4 mm thickness a four times higher death rate.
- more than 5 mitoses/10 high power fields is associated with poor prognosis
- lack of lymphocytic host response is associated with poor prognosis
- lymphatic, vascular, or perineural invasion are also associated with poor prognosis

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