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Cystic Benign Melanosis of the Conjunctiva

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Abstract

Purpose—To report the clinical and histologic features of cystic benign melanosis.

Methods—This case series reports on the clinical and histopathologic features of three patients with enlarging cystic, brown pigmented conjunctival lesions.

Results—Slit lamp exam showed cystic melanotic lesions of bulbar conjunctiva. Histopathologic examination of the biopsy specimens showed epithelial lined cysts in the substantia propria, goblet cells, and secondary pigmentation of basilar keratinocytes.

Conclusions—Cystic benign melanosis, a unique conjunctival lesion, should be differentiated from cystic nevus and primary acquired melanosis (PAM).

Keywords

conjunctiva; benign melanosis; cystic melanosis; epithelial inclusion cyst; racial melanosis

Introduction

Brown hyperpigmented conjunctival lesions can be separated into two broad clinical categories: benign and malignant. Clinical suspicion is formulated at the slit-lamp, and definitive diagnosis is made by histopathologic examination of tissue biopsy. Since conjunctival hyperpigmentation is common and, in some instances, may represent melanoma, it is important for ophthalmologists to be familiar with the spectrum of these lesions. Melanocytic tumors comprise 53% of all excised conjunctival lesions in a referral pathology laboratory¹. Melanotic lesions of the conjunctiva include racial melanosis, nevus, primary acquired melanosis (PAM), and melanoma^{1,2}.

The most common benign conjunctival lesions are due to racial (secondary) melanosis. Racial melanosis is present in 92.5% of African Americans, 35.7% of Asians, 28% of

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Hispanics, and 4.9% of Caucasians³. This benign entity is the result of epithelial melanocytes producing excessive melanin which is transferred into surrounding keratinocytes. Typically racial melanosis is bilateral, asymmetric, occurs in the interpalpebral fissures, and does not contain cysts⁴.

The most commonly biopsied benign pigmented conjunctival lesion is the nevus^{2,5}. Nevi do not involve the cornea, fornices, or palpebral conjunctiva and are well defined and mobile over the sclera. A nevus is a hamartomatous growth of any element of the epithelium. Nevi often contain cysts - a fairly specific feature of the compound nevus⁴. Nevi rarely may undergo malignant transformation to melanoma^{2,4}.

Primary acquired melanosis is a premalignant or malignant growth². Unlike nevi, PAM occurs later in life, is usually unilateral. It is flat, variably brown and lacks well-defined edges. PAM may involve the cornea epithelium, fornices, and the palpebral conjunctiva. In contrast to racial melanosis, PAM typically occurs in people with fair skin. PAM requires biopsy for evaluation of malignant potential. Histopathologically, PAM is divided into PAM with or without atypia⁶.

Cystic benign melanosis (CBM), which is reported here, has features of racial melanosis, cystic nevus, and PAM but it is histopathologically distinct. In a previous case report of CBM, Hutchinson et al reported bilateral circumferential perilimbal CBM in twins⁷. The pigmented lesions were located on the bulbar conjunctiva adjacent the limbus and were growing. Histopathology and electron microscopy showed epithelial lined cysts in the substantia propria and secondary pigmentation of basilar keratinocytes.

Recently, we examined three additional patients with cystic pigmented bulbar conjunctival lesions. Clinical features worrisome for malignancy prompted excisional biopsy and histopathologic examination proved them to be CBM. This report further defines the clinical and histologic spectrum of this entity.

Case Reports

Case 1

A 20-year-old black woman presented with a seven year history of a dark lesion in her right eye. Slit-lamp examination showed a cystic pigmented mass in the right temporal bulbar conjunctiva as well as mild arcus (Figure 1). Some of the cysts contained brown colored fluid. Excisional biopsy was performed. Histopathologic analysis showed epithelial inclusion cysts within the substantia propria and secondary pigmentation of the epithelium within the cysts as well as in the basilar keratinocytes. Some of the epithelial inclusion cysts were nearly full of epithelial proliferations while others contained proteinaceous material. No nevus cells were present. Immunohistochemical stains for S-100 were performed and failed to demonstrate any melanocytic proliferations. Follow-up exam two months after the biopsy showed no recurrence or enlargement of the cystic melanosis and the patient has since been lost to follow-up.

Case 2

A 66-year-old Native American woman presented with a ten year history of increasing brown pigmentation of the conjunctiva of her right eye. She also had a subtle tan pigmentation of the left eye which had been stable for many years. She had a history of chronic retinal detachment, remote cataract extraction, strabismus surgery, and band keratopathy in the right eye resulting in no light perception vision. Slit lamp examination of the right eye revealed multi-focal cystic and pigmented areas concentrated on the superior and inferior bulbar conjunctiva (Figure 2). Due to recent growth and concern for potential

malignancy, the lesions were biopsied and pathologic examination showed multiple epithelial inclusion cysts in the substantia propria and secondary pigmentation in the basilar keratinocytes. Immunohistochemical stains for S-100 failed to demonstrate melanocytic proliferations. At the most recent examination, eighteen months after biopsy, the lesions were stable.

Case 3

A 77 year-old black man was referred for evaluation of progressive dark brown conjunctival pigmentation of both eyes, more so on the left than the right. Slit lamp examination showed melanosis throughout the bulbar conjunctiva. The left eye had extensive abnormal dark brown pigmentation of the conjunctiva concentrated at the superior and temporal limbus containing small subconjunctival cysts. Prominent striate melanokeratosis was present throughout the cornea extending into the visual axis (Figure 3). Due to concern for potential malignancy, a biopsy of the conjunctival lesion was performed. Histopathologic analysis showed pigmentation of the basilar keratinocytes and epithelial inclusion cysts within the substantia propria. There was secondary pigmentation of the basilar keratinocytes in the epithelial inclusion cysts. Immunohistochemical stains for S-100 did not demonstrate melanocytic proliferations. At the last follow-up appointment, fifteen months after the biopsy, the cystic melanosis was unchanged.

Discussion

This case series reports three new cases of cystic benign melanosis. All three patients had darkly pigmented skin, two were black and one was Native American. The condition was unilateral in one case (case 1), and bilateral in two cases with marked asymmetry. The lesion was of childhood onset in case one, and the other two cases began during adulthood. All three cases displayed slowly growing pigmented lesions concerning for malignancy that prompted biopsy.

Hutchinson et al reported black twin sisters with bilateral light brown pigmentation of the bulbar conjunctiva just outside the limbus⁷. Electron microscopy showed melanocytes in the substantia propria and melanin granules in the cytoplasm of epithelial cells. None of the five total reported specimens of CBM contained nesting cells or nevus cells.

CBM and cystic nevus share several features (Table 1). Similar to CBM, cysts are a common feature of conjunctival nevi^{2,4}. Approximately 50 to 65% of conjunctival nevi contain cysts^{2,9}. Both CBM and nevi may be elevated, and often occur in childhood. CBM and cystic nevi may grow over time, but nevi classically grow during times of hormonal stimulation⁴.

CBM and the cystic nevus are distinctly different entities. While both contain epithelial lined cysts and share other clinical features, they differ clinically in that CBM has less well-defined edges and may involve the cornea epithelium. Additionally, the pigment in CBM is from secondary melanosis of the basilar keratinocytes from epithelial melanocytes, while the pigment in a melanocytic nevus is from hamartomatous proliferation of epithelial melanocytes with deposition of melanin into neighboring keratinocytes. Immunohistochemical stains for S-100 were performed in all three of our cases and failed to demonstrate any melanocytic proliferations, confirming that the lesions represent secondary pigmentation of the epithelium and not an increase in melanocytic cells. Perhaps most importantly, CBM does not contain nevus cells.

CBM also shares some clinical features with PAM (Table 1). Both entities may present in middle-aged patients, and both display poorly defined edges and potential involvement of

the cornea epithelium⁶. CBM should be rather easily differentiated from PAM, as CBM is elevated and inherently contains cysts.

Case two requires special discussion due to the surgical history. The melanosis and cysts may have been prompted by incisions from cataract or strabismus surgery, but there are more cysts than would be expected in a surgical wound. Furthermore, the location of the melanosis and cysts are most dense in the superior and inferior bulbar conjunctiva, while the strabismus surgery involved only horizontal muscles. The cataract extraction likely involved a large superior scleral tunnel. Regardless, this case of cystic benign melanosis is quite unusual and was histopathologically similar to the other cases. Jahnle et al reported a similar finding in a black patient with racial melanosis and a unilateral pigmented conjunctival mass that clinically simulated melanoma⁸. That patient presented six years after extracapsular cataract extraction with a fornix based flap. Histology revealed substantia propria cysts associated with melanocytic hyperpigmentation of the basilar cell layer of the epithelium as well as hyperpigmentation of the inclusion cyst lining.

CBM is a secondary melanosis with pigmented cystic inclusions that may be highly asymmetric. Prior inflammation of epithelial and goblet cells may cause sequestration into the substantia propria which subsequently forms cysts. Less likely, CBM could represent nevi where all nesting cells have regressed leaving behind substantia propria cysts and melanocytic pigmentation.

CBM is most analogous to benign racial melanosis with the unusual addition of subepithelial cysts. With increasing awareness of this unique entity and its differences from other brown pigmented conjunctival lesions, more knowledge regarding the natural history, clinical behavior, and heredity will be gained. Nonetheless, our cases indicate that CBM has no malignant potential and does not warrant further treatment after establishment of the diagnosis.

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Figure 1.

Case 1. Top. There is a raised, cystic, pigmented lesion on the temporal bulbar conjunctiva. Some of the cysts contain fluid. Middle. The lesion is composed of epithelial inclusion cysts in the substantia propria. Bottom. Some of the basilar keratinocytes of the cysts are secondarily pigmented with melanin pigment. (hematoxylin and eosin, middle 25X, bottom 100X)

Figure 2.

Case 2. Top left. There is a patchy, pigmented cystic lesion in the superior-nasal bulbar conjunctiva. Top right. There is secondary pigmentation of basilar keratinocytes in the epithelium and within epithelial inclusion cysts in the substantia propria. Bottom left. Some of the epithelial inclusion cysts are filled with proliferations of epithelium. Bottom right. Other epithelial inclusion cysts contain proteinaceous material in their lumens. (hematoxylin and eosin top right 25X, bottom right and left 100X)

Figure 3.

Case 3. Top. Abnormal pigmentation of the conjunctiva at the superior and temporal limbus with extension into the bulbar conjunctiva. Prominent striate melanokeratosis is present throughout the cornea extending into the visual axis. Middle. There is secondary pigmentation of the basilar keratinocytes and an epithelial inclusion cyst in the substantia propria. Bottom. There is secondary pigmentation in the basilar keratinocytes in the epithelial inclusion cyst. (hematoxylin and eosin, middle 25X, bottom 100X)

Table 1

	Cystic Benign Melanosis	Cystic Nevus	Primary Acquired Melanosis
<u>Clinical Findings</u>			
Age of onset	childhood to middle-age	childhood	middle-age to elderly
Location	bulbar conjunctiva	bulbar conjunctiva	bulbar, forniceal, or palpebral conjunctiva
Laterality	unilateral or bilateral	unilateral or bilateral	unilateral
Elevated	yes	junctional: no compound: yes subepithelial: yes	no
Cornea Involvement	yes	no	yes
Growth	slow	variable	variable
Malignant Potential	none	yes	yes
Well-defined Edges	no	yes	no
Cysts	Inherently yes	Inherently yes	no
<u>Pathologic Findings</u>	epithelial lined cysts in the substantia propria, goblet cells, secondary pigmentation of basilar keratinocytes	nests of junctional, compound, or subepithelial nevus cells, sometimes epithelial-lined cysts	without atypia: bland melanocytes confined to basilar epithelium with atypia: atypical melanocytes with abnormal growth patterns