Primary Acquired Melanosis: Clinical, Histopathologic and Optical Coherence Tomographic Correlation

Yahya A. Alzahrani^a Smita Kumar^a Hassan Abdul Aziz^a Thomas Plesec^b
Arun D. Singh^a

^aDepartment of Ophthalmic Oncology, Cole Eye Institute, and ^bAnatomic Pathology, Cleveland Clinic, Cleveland, Ohio, USA

Key Words

Corneal epithelium · Correlative microscopy · Immobilization stress · Melanoma · Noninvasive diagnostic tool · Optical coherence tomography

Abstract

Aim: To assess the use of anterior segment optical coherence tomography (OCT) as an adjuvant diagnostic tool in primary acquired melanosis (PAM) by correlating clinical, histopathologic and anterior segment OCT findings. **Methods:** Twenty-four patients (24 eyes) with PAM of the conjunctiva, cornea or both were imaged with an anterior segment OCT device (RTVue, model-RT100; Optovue Inc., Fremont, Calif., USA). **Results:** Histopathologic diagnosis following excisional or incisional biopsy was confirmed in 13 out of 24 patients (54.6%). OCT images showed a characteristic uniformly thick basal epithelial hyperreflective band (about 20 μ m thick) and normal thickness of the overlying epithelial layer in all patients (100%). The hyperreflective band on OCT correlated with the basal epithelial melanocytic pigmentation noted on histopathologic examination but did not vary in thickness between cases with or without atypia. **Conclusions:** The characteristic basal epithelial hyperreflective band with normal overlying epithelium in the absence of cysts observed in

all cases by anterior segment OCT correlated with clinical and histopathologic features of conjunctival and corneal PAM. Anterior segment OCT may be helpful as a noninvasive diagnostic tool for PAM. Improvement in resolution is necessary to detect melanocytic hyperplasia and atypia suggestive of malignant potential.

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Introduction

Conjunctival primary acquired melanosis (PAM) is an acquired flat, painless noncystic pigmented lesion of the conjunctiva [1, 2]. PAM usually occurs unilaterally in middle-aged individuals (mostly Caucasians) and accounts for 11% of all conjunctival tumors and for 21% of all conjunctival melanocytic lesions [2]. It can either be regarded as benign (PAM without atypia) or as a precancerous lesion (PAM with atypia) [3–7]. More recently, the spectrum of histopathologic features within PAM has been emphasized rather than an absolute distinction between PAM without or with atypia [8]. Histopathologically, PAM without atypia is best characterized by melanocytic hyperpigmentation along the basal epithelial layer of the conjunctiva, while atypia refers to melanocytic

hyperplasia comprised of isolated or confluent nests of atypical melanocytes [3, 5, 7].

Anterior segment OCT is a relatively new diagnostic tool that is being investigated for various anterior segment disorders [9]. Spectral domain OCT offers higher resolution of approximately 5 μm compared to time domain OCT, with a resolution of 10–18 μm [10–13]. Spectral domain OCT has been investigated as adjunct in the management of ocular surface lesions for diagnosis, treatment planning and monitoring of response [9, 14–16].

As conjunctival or corneal PAM may be subtle and difficult to document on clinical examination and by conventional photography, we have investigated the role of a commercially available spectral domain anterior segment OCT device in detecting PAM by investigating the correlation of clinical, histopathologic and OCT findings.

Patients and Methods

This case series included 24 eyes of 24 consecutive patients with a clinical diagnosis of conjunctival or corneal PAM. All patients underwent complete ophthalmic examination. After the initial clinical diagnosis was made, slit lamp examination and anterior segment OCT imaging were performed with a commercially available device (RTVue, model-RT100; Optovue Inc., Fremont, Calif., USA), with a resolution of 5 μm [26,000 A-scan(s)] and using a wavelength of 840 nm. Horizontal or vertical scans of the lesions were acquired. Thirteen patients out of 24 underwent excisional or incisional biopsy to confirm the diagnosis.

Results

Twenty-four eyes of 24 patients with a clinical diagnosis of conjunctival/corneal PAM were included in this study. There was a female predominance (15 females vs. 9 males). The mean age was 64 years (range 31–94). Clinical findings included a patch of flat, ill-defined pigmented epithelial lesions noticed on slit lamp examination (100%; fig. 1a, 2a). Nineteen patients (79.6%) had only conjunctival involvement, while in 4 patients (16.6%), the pigmentation was extend across the limbus into the adjacent cornea (fig. 3), and 1 patient (4.16%) had isolated corneal PAM. Conjunctival cysts were absent in all patients (100%). Eleven patients (45%) were observed without biopsy or chemotherapy because the lesion was small, stable over follow-up, or the patient was asymptomatic.

Histopathologic specimens of 13 patients (55%) who underwent excisional or incisional biopsy were studied.

Fig. 1. a Localized conjunctival PAM without atypia. **b** Note the basal epithelial hyperreflective band of approximately 20 μm thickness (arrow, above) and the corresponding melanocytic hyperpigmentation that is restricted to the basal layer (below). HE. $\times 200$.

The specimens showed melanocytic hyperpigmentation within the basal layer of the epithelium in all cases (fig. 1b, 2b). Nine out of 13 patients (69%) additionally showed melanocytic hyperplasia which is compatible with the diagnosis of PAM with atypia (fig. 4b), characterized by cytological (nuclear enlargement, prominent nucleoli and abundant cytoplasm) and architectural atypia (melanocytic extension of the basal layer and nesting of cytologically atypical melanocytes), while 4 patients (31%) showed only melanocytic hyperpigmentation without cytologic or architectural atypia, indicative of PAM without atypia (fig. 1b, 2b). Stromal extension or invasive melanoma and conjunctival cysts were absent in all histopathologic samples (100%).

Anterior segment OCT demonstrated a uniformly thick basal epithelial hyperreflective band in all cases

Color version available online

Fig. 2. **a** Diffuse conjunctival PAM without atypia. **b** Note the basal epithelial hyperreflective band of approximately 20 μm thickness (arrow, above) and the corresponding melanocytic hyperpigmentation that is restricted to the basal layer (below). HE. $\times 200$.

(100%; fig. 2b, 3, 4b). The overlying epithelium was normal in all patients (100%). Optical shadowing (partial or total) of subepithelial layers was observed in 6 patients (25%). Conjunctival cysts were absent in all patients (100%).

The histopathology of examined specimens showed a high correlation with the OCT findings. Cases of PAM sine pigmento were not observed in this series. The melanocytic hyperpigmentation within the basal layer of the epithelium correlated with the hyperreflective band observed on anterior segment OCT (fig. 1b, 2b). Also, normal overlying epithelium and the absence of conjunctival cysts, observed on clinical and histopathologic evaluation, correlated with the OCT findings (100%). Optical shadowing noted on OCT correlated with the amount of melanocytic pigmentation observed on the histopatho-

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Fig. 3. Corneal PAM. **a** Clinical appearance. **b** Note the corresponding epithelial hyperreflective band (arrow).

Color version available online

Fig. 4. **a** Localized conjunctival and corneal PAM with atypia. **b** Note the round stromal hyperreflective zone (arrows, above) with similar appearance of an atypical melanocytic nest (arrows, below). HE. $\times 200$. Without point-to-point correlation between the OCT and the histopathologic image, no definite correlation can be derived.

Table 1. Conjunctival melanocytic lesions: comparison of typical anterior segment OCT features

Diagnosis	Epithelial hyperreflective band	Stroma	Shadowing	Cyst
PAM	+++	normal	+/-	absent
Nevus	++	normal/abnormal	++	present
Melanoma	+	abnormal	+++	absent

logic sample. It was not possible to differentiate cases of PAM with atypia from those without atypia by OCT as the hyperreflective band did not vary in thickness between the cases with or without atypia. However, in 1 case with melanoma in situ (PAM with atypia), an atypical melanocytic nest observed on histopathology showed a similar appearance on OCT (fig. 4b).

Discussion

Anterior segment OCT imaging technology provides a noninvasive adjunct diagnostic tool to the gold standard histopathology specimen in ocular surface lesions such as ocular surface squamous neoplasia [14–18]. Limited studies have investigated other conjunctival lesions such as nevi and melanoma [17, 18]. We have analyzed the correlation of clinical, histopathologic and OCT findings of conjunctival and corneal PAM using a commercially available spectral domain anterior segment OCT device.

The characteristic features of PAM (with or without atypia) observed in our series include a uniform basal hyperreflective band of approximately 20 μ m thickness (100%) with normal overlying epithelium and absence of cysts in all cases (100%). Our observations are similar to those reported by Abou Shousha et al. [14] and Nanji et al. [18] who reported an epithelium of normal thickness and a regular hyperreflectivity of the basal epithelium with the use of ultra-high- and high-resolution OCT in 8 and 8 cases, respectively [14, 18]. Cases of PAM sine pigmento were not observed in this series. In such rare cases, there would be no hyperreflective band on OCT, with or without epithelial thickening.

In contrast to PAM, conjunctival nevi characteristically have a high likelihood of conjunctival cysts (77–100%) [17] with normal epithelium [17, 18]. Both PAM and nevi have an epithelial layer of normal thickness on OCT [14, 18]. In contrast, conjunctival melanoma ap-

pears as a hyperreflective, thickened epithelium with extension of hyperreflectivity into the subepithelial layer and significant optical shadowing which may obscure the underlying tissue [14, 18]. Characteristically, cysts are absent in melanoma on OCT [18]. Comparative OCT findings of conjunctival and corneal melanocytic lesions are summarized in table 1.

Optical shadowing is a major limitation of anterior segment OCT. The identification of the posterior extent of the lesion can be obscured by optical shadowing, which is directly influenced by the extent of melanocytic pigmentation and the thickness of the lesion, and hence, limits the use of OCT for full characterization of the nevus or melanoma, as they tend to thicken. The corneal epithelium [17] PAM, which tends to be flat by clinical criteria, is less susceptible to this limitation, as observed in this study. An additional limitation of the anterior segment OCT device used in this study was its inability to differentiate cases of PAM with atypia from those without atypia, as the hyperreflective band did not vary in thickness between the cases with and those without atypia. Meticulous studies with point-to-point correlation between the OCT and histopathologic images are required before any definite conclusions regarding the ability of OCT to detect histopathologic atypia can be reached (fig. 4). Nevertheless, anterior segment OCT is an excellent tool for imaging the anterior surface and lateral extent of the lesions.

In summary, the characteristic basal epithelial hyperreflective band with a normal overlying epithelium in the absence of cysts observed in all cases by anterior segment OCT correlated with clinical and histopathologic features of conjunctival and corneal PAM. Anterior segment OCT may be helpful as a noninvasive diagnostic tool for PAM. Improvement in resolution is necessary to detect intraepithelial melanocytic hyperplasia (atypia) suggestive of malignant potential.

Statement of Ethics

The study protocol has been approved by the Institute's Committee on Human Research. The study application was approved as Exempt Research by the Institutional Review Board for the collection of data in an anonymous manner in which participants were not identifiable.

Disclosure Statement

The authors declare no conflicts of interest.

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