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Potential utility of dermoscopy in the examination of ocular pigmentations

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ABSTRACT

Background: Dermoscopy is a fundamental method in the examination of melanocytic neoplasms. Limited data exist about the dermoscopic features of ocular pigmentations (OPs).

Objectives: We aimed to investigate the usefulness of dermoscopy in the examination of OPs.

Methods: Dermoscopic images of OPs of 20 consecutive patients were recorded. Impression cytology (IC) was performed to these lesions. Dermoscopic images were evaluated for specific dermoscopic structures and patterns without knowing the cytological examination results.

Results: Fifteen percent (3/20) of the lesions presented with suspicious cytological findings. More of the suspicious lesions had 4 colors compared to benign lesions (66.7% vs 11.8%, p=0.088). This was also determined for blue-gray (66.7% vs 11.8%, p=0.088) and white (66.7% vs 17.7%, p=0.14) colors. At least 3 structures were observed in all suspicious lesions (100%), but were observed in only in 41.2% of benign lesions (p=0.105). Besides, two-thirds of suspicious lesions had more than 4 structures, but none of the benign lesions reported this (p=0.016). Most of the benign lesions showed asymmetry in one axis (93.3%), whereas all suspicious lesions showed asymmetry in 2 axes (p=0.004).

Conclusions: Dermoscopy seems to be a useful method in the evaluation of OPs. The existence of dermoscopic patterns, colors, and dermoscopic structure plurality and asymmetry raise suspicion in OPs, similarly to skin pigmentations. Dermatologists should be aware of the ocular area, and closer collaboration should be developed between dermatologists and ophthalmologists in the management of pigmented lesions.

Introduction

The ocular surface includes the conjunctiva and the cornea. Specifically, melanocytic lesions that arise in this area are melanocytic nevus, racial melanosis, primary acquired melanosis, and melanoma. Melanocytic nevi are the most common melanocytic tumors of the conjunctiva. They generally become clinically evident during the first and second decade of life. Typically, the conjunctival melanocytic nevi are pigmented, well defined, and elevated lesions. Approximately 1% of melanocytic nevi evolve to melanoma. Racial melanosis presents commonly on the limbus as bilateral congenital, circular pigmentation. Ocular melanocytosis is also a congenital pigmentation status entertaining a melanoma risk; it emerges unilaterally and involves periocular skin, the sclera, and orbita, but typically spares conjunctiva. Ocular melanocytosis is commonly confused with primary acquired melanosis, which is an acquired condition emerging in middle age that presents with diffuse, patchy, poorly defined, and flat pigmentation. Thirteen percent of primary acquired melanosis lesions with atypia can also give rise to melanoma [1-3]. The reasons for conjunctival nevi excisions include fast growth, suspicious changes under biomicroscopic examination such as intrinsic vascularity and/or pigmentation increase, cosmetic reasons, and patient concerns about malignancy [1,2,4]. Ocular melanoma arises from melanocytes within the eye, including the uveal tract, conjunctiva, and orbit; it constitutes less than 5% of all melanoma cases. Conjunctival melanomas comprise only ~5% of ocular melanomas; however, the incidence has been increasing, as reported for cutaneous melanoma, which is being related to ultraviolet light exposure [5,6]. The rarity of conjunctival melanomas contributes to difficulties in their management.

Slit-lamp biomicroscopy, high-resolution anterior segment ultrasound, in vivo confocal microscopy, and optical coherence tomography constitute the noninvasive diagnostic technologies for evaluating ocular surface lesions [7]. Dermoscopy is one of the most important noninvasive technologies being used in the diagnosis and follow-up of pigmented skin lesions [8]. In the present study, we aimed to investigate the usefulness of dermoscopy in the examination of ocular pigmentations (OPs).

Materials and Methods

Patients with ocular pigmentation older than 18 years old who presented to the Departments of Dermatology and Ophthalmology of the Faculty of Medicine of Pamukkale University between December 2010 and March 2012 were invited to participate in the study, prospectively. The lesions were examined clinically and dermoscopically. Dermoscopic images were taken with a DermLite Pro HR (polarizing) handheld dermatoscope (3Gen, San Juan Capistrano, CA) coupled with a Sony Cyber-Shot DSC-W35 camera (Sony Corporation, Zug, Switzerland) after removing the glass faceplate. The polarizing technology of the dermatoscope used in the present study allowed us to take dermoscopic images from a distance of approximately 1 cm without contact with the lesions.

Impression cytology (IC) was performed on these lesions after dermoscopic imaging. Sampling was performed as follows: the eye was anesthetized with 1-2 drops of 0.5% proparacaine HCL (Alcaine) and the eyelids were opened for a few seconds to dry the conjunctiva to improve the adherence of cells to the cellulose acetate filter paper with a pore size of 0.45 (m. The cellulose acetate filter paper was pressed gently onto the surface of the OP; after 3-5 seconds, it was removed. The procedure was repeated 2-3 times to increase the sensitivity of the technique. The cellulose acetate filter paper was immediately fixed in 95% ethanol for 15 minutes and stained by the Papanicolaou method, which was performed on the same day of collection. At this stage, the filter paper was placed in position with the cell sample facing upward during staining, avoiding contamination and loss of material. After the coloration, it was mounted with Entellan (Millipore Sigma, Darmstadt, Germany) and filter paper on the slide.

IC samples were screened in terms of nuclear size, nuclear-to-cytoplasmic ratio, irregular nucleus, irregular nuclear chromatin pattern, and prominent nucleoli, and subsequently graded into 4 different stages: 0 (insufficient material for diagnosis), 1 (normal epithelial conjunctival cells with or without melanin pigment, reactive conjunctival cells as seen in inflammation), 2 (melanocytes with mild atypia), 3 (melanocytes with moderate atypia), and 4 (melanocytes with severe atypia) [9]. The amount of cells collected (low, moderate, high, very high) was noted for all samples [10].

The lesions with grade 1 or 2 atypia on IC samples were regarded as benign and those with grade 3 or 4 atypia as suspicious. Grade 0 IC samples were not taken under consideration [11]. Dermoscopic images were evaluated for specific dermoscopic structures and patterns by one of the authors (NK) without prior knowledge of the cytological examination results.

Fisher's exact test was used for statistical analyses with SPSS software (version 18.0; SPSS Inc, Chicago, IL, USA). P values < 0.05 were considered significant.

Power analysis was performed according to these results (for more than 4 structures, suspicious 66.7% and benign 0%) and it was determined that the present study had more than 80% power with 95% confidence.

For the present study approval was obtained from the Medical Research Ethics Committee of the Faculty of Medi-

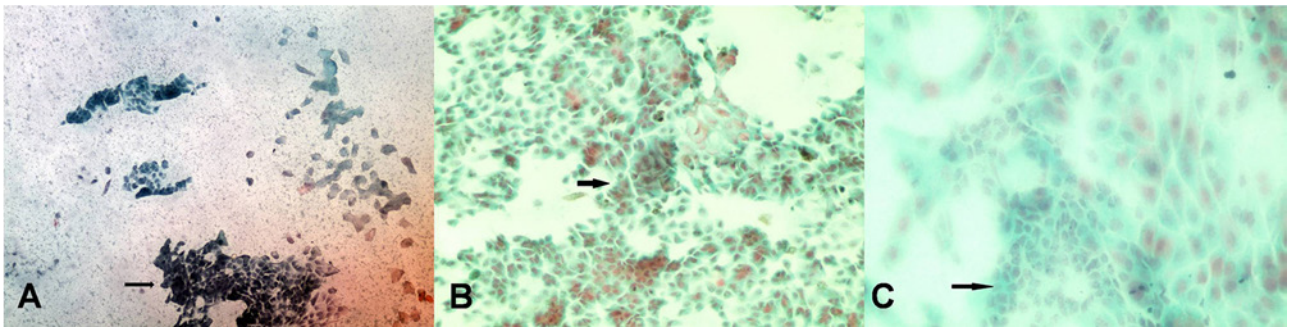

Figure 1. Cytological examination of the suspicious lesions of the 3 cases showing grade 4 atypia in the sheets of atypical melanocytes. (A) PAP ×10 and grade 3 atypia. (B) and (C) PAP ×20. [Copyright: ©2018 Kaçar et al.]

cine, Pamukkale University, and all participants gave their informed consent.

Results

The study enrolled 24 OPs from to 23 patients. Four lesions of 3 patients were excluded because IC samples were grade 0 (insufficient material for diagnosis). Twenty OPs of 20 patients (12 males, 8 females) were included in total. The clinical diagnoses, based on clinical features including the localization, onset time, and morphological characteristics of the lesion and biomicroscopic findings were primary acquired melanosis in 6 lesions, Ota nevus in 1, melanocytic nevus in 12, and melanoma in 1 lesion. Three lesions showed grade 3 atypia (Figure 1). Two of the 3 cytologically suspicious lesions were clinically diagnosed as melanocytic nevus; only 1 was suspicious from the clinical point of view. Biopsy was planned for these lesions; however, the patients did not agree. Two cytologically benign lesions could be followed up, and no change was observed in them when comparing their cytological diagnosis (Figure 2). Another cytologically benign lesion was removed at the request of the patient and the histopathological diagnosis was compound nevus.

Homogeneous and globular patterns were the dominant dermoscopic patterns in both benign lesions (seen in 14 and 13 lesions, respectively) and suspicious (3) lesions (Figure 3). These patterns coexisted in most of the lesions

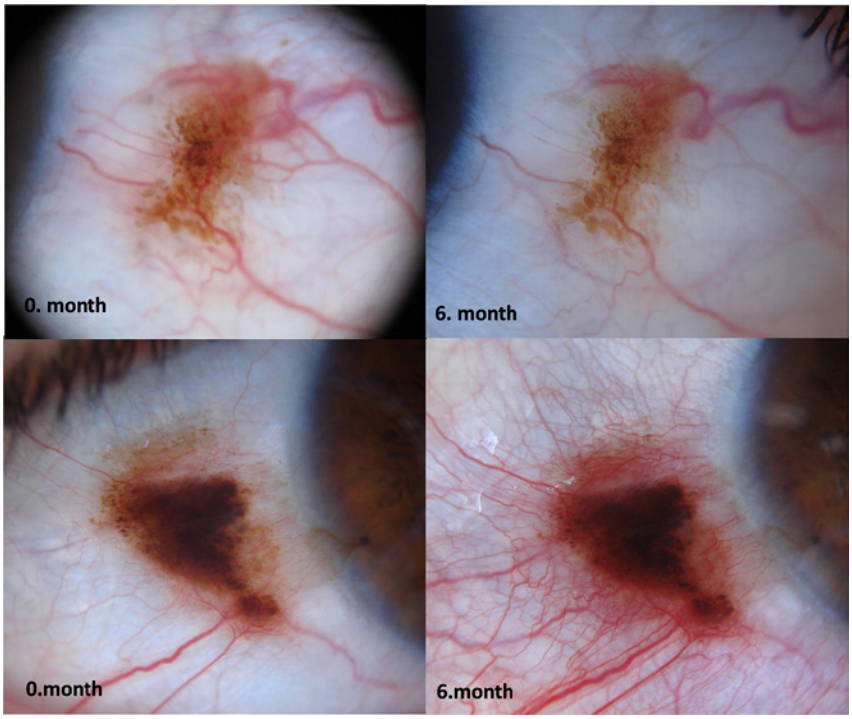

Figure 2. No dermoscopic changes were observed within 6 months in the 2 observed lesions. [Copyright: ©2018 Kaçar et al.]

(65%). Only 1 pattern was found in 6 (all benign), 2 patterns in 13 (11 benign, 2 suspicious) and 3 patterns in 1 lesion (suspicious).

We found 4 lesions with only a single color (all benign), 11 (10 benign, 1 suspicious) with 2 colors, 1 (benign) with 3 colors, and 4 (2 benign, 2 suspicious) with 4 colors. The most frequent color was light brown, which was present in 18 lesions (15 benign, 3 suspicious), followed by dark brown (16 lesions [13 benign, 3 suspicious]), white (5 lesions [3 benign, 2 suspicious]), blue-gray (4 lesions [2 benign, 2 suspicious]), and black (2 benign lesions). More of the suspicious lesions showed 4 colors compared to benign lesions (66.7% vs 11.8%, p=0.088). This was also determined for blue-gray (66.7% vs 11.8%, p=0.088) and white (66.7% vs 17.7%, p=0.14) colors. The most prevalent dermoscopic structure was the structureless area observed in 17 lesions (14 benign, 3 suspicious), followed by dots (13 benign, 3 suspicious), globules (11 benign, 3 suspicious), pigment network (1 benign, 2 suspicious) and streaks (1 benign, 2 suspicious).

Only one dermoscopic structure was found in 1 lesion (benign), 2 struc-

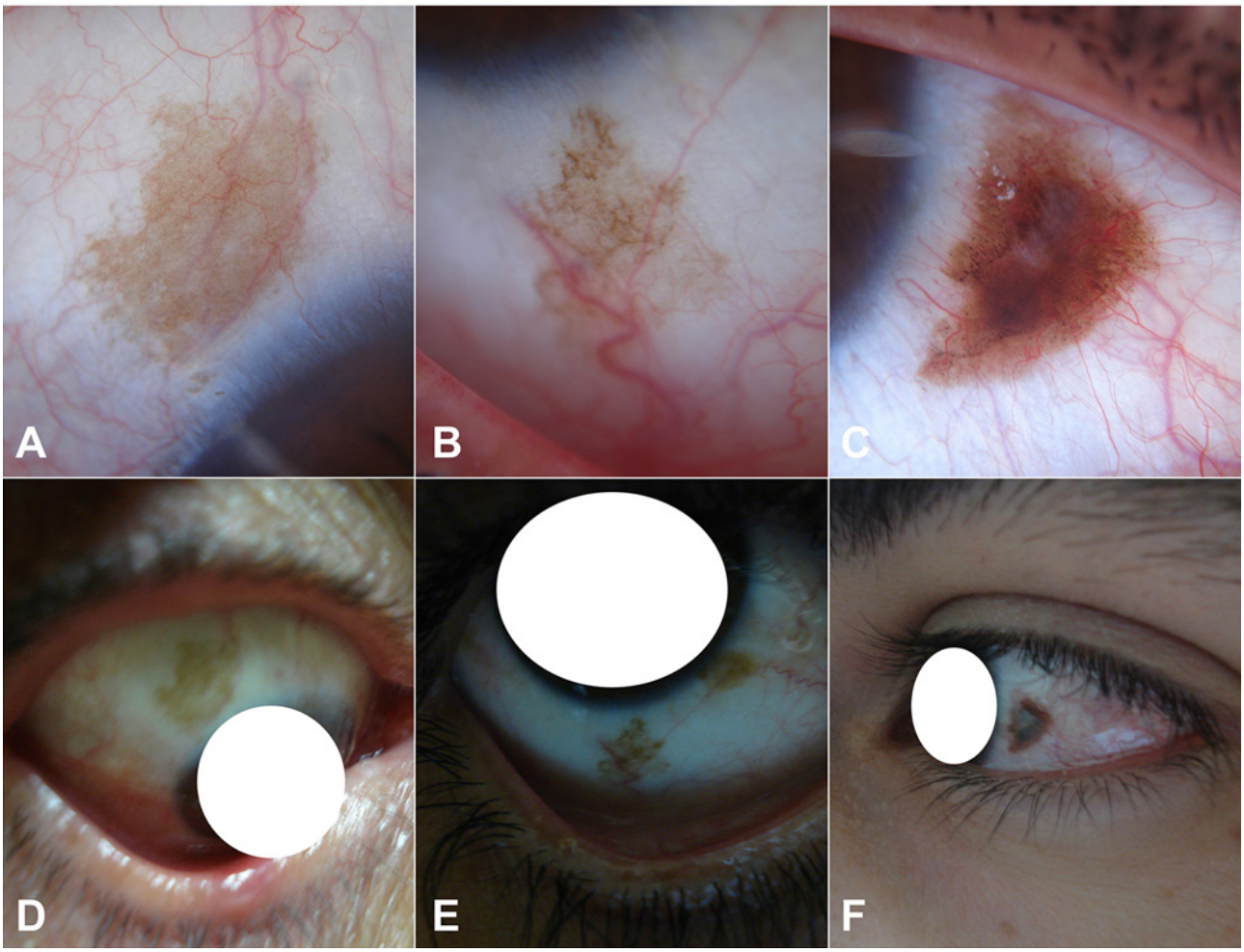

Figure 3. (A), (B), and (C) Dermoscopic views of some OPs (original magnification ×10): (A) homogeneous, (B) reticular, and (C) homogeneous-reticular dermoscopic patterns. (D), (E), and (F) Clinical views of some OPs. [Copyright: ©2018 Kaçar et al.]

tures in 9 lesions (all benign), 3 structures in 8 lesions (7 benign, 1 suspicious), 4 structures in 1 lesion (suspicious), and 5 structures in 1 lesion (suspicious). Three or more structures were observed in all suspicious lesions (100%), but in only 41.2% of the benign lesions (p=0.105). Two-thirds of suspicious lesions had more than 4 structures, but none of the benign lesions had this (p=0.016). Asymmetry was observed in all lesions except for 2 benign ones (90%). Most of the benign lesions showed asymmetry in one axis (93.3%), whereas all suspicious lesions showed asymmetry in 2 axes (p=0.004). Categorical comparisons are summarized in Table 1.

Discussion

The fields of dermatology and ophthalmology overlap in many ways, as a number of diseases involve both the eye and the skin. One of those diseases is melanoma. Dermatologists have an important place in the management of skin melanoma. It has been established that the early detection of melanoma is the most effective intervention to improve prognosis [11]. Dermoscopy is a fundamental method in the examination of melanocytic neoplasms. It has been established that dermoscopic examination increases the diagnostic accuracy from 5% to 30% [10]. The whole skin, nails, and mucosa should be examined during melanoma screening. Although nails and oral and genital mucosa lesions have been routinely examined in addition to skin, dermatologists generally do not show interest in ocular mucosa. Therefore, there are not much data about the dermoscopic features of pigmentations on ocular mucosa in the literature. We observed light-brown-colored homogeneous pattern, a benign dermoscopic pattern [12], in the conjunctival pigmentation of a case of Laugier-Hunziker syndrome. IC of the pigmentation revealed melanocytes with only a mild atypia, suggesting a benign nature in accordance with the dermoscopic pattern we observed [13]. Atypical pigment network, irregular dots/globules, regression structures, and blue-white veil, all of which are melanoma-specific dermoscopic features, were reported in a case of palpebral conjunctival melanoma. Concordance was present between dermoscopic findings and diagnosis in that case as well [14].

TABLE 1. Categorical Comparisons

Dermoscopic Features	Benign	Suspicious	P value
≥4 colors	11.8	66.7	=0.088
Blue-gray color	11.8	66.7	=0.088
White color	17.7	66.7	=0.14
≥3 structures	41.2	100	=0.105
≥4 structures	0	66.7	=0.016
Asymmetry in 2 axes	5.9	100	=0.004

Homogeneous, globular, starburst, and reticular patterns are the dermoscopic patterns seen most frequently in benign pigmented skin tumors. The presence of more than 2 dermoscopic patterns together suggests malignant nature. In addition, the presence of color and/or dermoscopic structure multiplicity and/or asymmetry also raises suspicion [12]. In the present study, we found that 4 colors, 3 or more dermoscopic structures, asymmetry in 2 axes, and blue-gray or white colors are the dermoscopic findings that indicate a suspicious lesion. According to our results, dermoscopic pattern, color, and dermoscopic structure plurality and asymmetry should arouse suspicion in OPs, similarly to skin pigmentations. Particular attention should be paid to lesions with more than 4 structures and/or asymmetry in 2 axes.

There are 2 limitations of our study. First, the sample size of our study is relatively small. Second, we only performed IC for the lesions. IC is an extensively used method to evaluate superficial epithelial layers of the ocular surface [7]. It was demonstrated that IC with cellulose acetate filters is able to sample deeper layers when performed repeatedly [15]. The major advantage of IC is to preserve the eye from unnecessary surgical procedures [7]. An increased nuclear-to-cytoplasmic ratio, an irregular nuclear chromatin pattern, the presence of large nucleoli, and the observation of mitosis and anisokaryosis have been suggested as malignant cytological features in melanin-containing cells [16]. Although the gold standard for diagnosis is histopathological examination, a 73% correlation was found between IC and histopathology in pigmented lesions from the conjunctiva, and biopore membrane IC was shown to accurately predict the outcome in 88% of the 127 histopathologically proven melanocytic lesions [16,17]. The positive and negative predictive accuracy of IC have been found to be 97.4% and 52.9%, respectively, when compared to histopathological findings in the diagnosis of ocular surface neoplasia [18]. In conclusion, IC was proposed to be a useful noninvasive method in evaluating conjunctival nevi [19]. In our study, the 2 observed lesions with benign cytological features showed no dermoscopic changes in comparison to their cytological diagnosis; in addition, histopathological diagnosis of another cytologically benign lesion that was removed at the request of the patient was also benign.

Conclusions

According to our knowledge, the present study is the first prospective study to investigate the dermoscopic features of OPs. Our results demonstrated that dermoscopy is a useful method in the examination of OPs. Dermatologists should be aware of the ocular area in terms of possible melanoma involvement, and closer collaboration should be developed between dermatologists and ophthalmologists in the management of pigmented lesions.

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