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Dermoscopic and histopathological correlation in macular hyperpigmented facial lesions

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Ethics Committee Approval

The study was conducted with the approval of the Ethics Committee of Clinical Research at Cukurova University (approval number: 2006/10-1). All procedures in this study involving human

participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Solar lentigo, seborrheic keratosis, actinic keratosis, lentigo maligna are confusable hyperpigmented lesions. Dermoscopy is an important tool to distinguish the pigmented lesions on the face. This study aimed to determine the reliability of dermoscopy by comparatively analyzing dermoscopic findings with the histopathologic examination of facial hyperpigmented flat lesions.

Methods: Patients with hyperpigmented flat lesions on the face such as solar lentigo, seborrheic keratosis, and actinic keratosis were included in this retrospective cohort study. Those with other causes of facial hyperpigmentation were excluded from the study, based on history, clinical evaluation, Wood's lamp examination, and dermoscopic findings. The dermoscopic criteria form, prepared for solar lentigo, seborrheic keratosis, actinic keratosis, and lentigo maligna were filled out. Biopsy was taken for histopathologic evaluation.

Results: Fifty-one patients, 26 males, and 25 females, with 53 skin lesions were evaluated. We did not statistically evaluate 3 lesions that had a histopathologic diagnosis of actinic keratosis + solar lentigo. The other 50 lesions' histopathologic diagnoses were actinic keratosis in 32 lesions, seborrheic keratosis in 9, and solar lentigo in 9. Kappa test was used for statistical analysis, which revealed a value of 0.645 (P<0.001). This shows that the dermoscopic and histopathological diagnoses of the hyperpigmented flat lesions on the face were moderately compatible.

Conclusion: Since the dermoscopic diagnosis of facial pigmented lesions cannot be based on the presence of one criterion, we deduce that histopathology is still the gold standard for accurate diagnosis.

Keywords: Actinic keratosis, Dermoscopy, Seborrheic keratosis, Solar lentigo

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Introduction

Facial diseases can cause pigmentation either during the natural course of the disease or secondarily. Ephelis, melasma, nevus of Ota, nevus spilus, Cafe au lait spots, drug eruption, post-inflammatory hyperpigmentation, photosensitive dermatitis, verruca plana, tinea versicolor, erythromelanosis follicularis faciei et colli, erythema dyschromicum perstans, Riehl melanosis, actinic lichen planus, lentigo simplex, solar lentigo, seborrheic keratosis, actinic keratosis, and lentigo maligna melanoma are among the diseases that can cause facial pigmentation [1]. Some of these lesions can be easily identified because of their significant clinical features. However, difficulties may be encountered in distinguishing lesions such as solar lentigo, seborrheic keratosis, actinic keratosis, and lentigo maligna from each other due to their overlapping clinical appearances. Since actinic keratosis and lentigo maligna are premalignant, they must be diagnosed and treated in the early stage [2, 3].

Dermoscopy, an in vivo, non-invasive method, aids in the differential diagnosis of skin lesions and early diagnosis of melanoma [4]. The use of dermoscopy helps in the classification of skin lesions as melanocytic or non-melanocytic, and the differentiation of benign and malignant lesions [5-7]. Recent studies demonstrated that dermoscopy increases the diagnostic accuracy of pigmented lesions by up to 5-30% [8, 9]. Kreusch and Rassner demonstrated that well-organized honeycomb pigmentation was replaced by a rough pigment network in the hyperpigmented lesions on the face independent from the deposition of melanin in the rete ridges. This structure is called a "pseudo-pigment network". Hypopigmented follicles or the orifices of the sweat glands perforate the hyperpigmented skin surface, and thus bright-colored openings are formed. A thick network structure with large holes is seen with the help of a dermoscopy [10]. Pseudo-network structure is a common finding in solar lentigo, lentigo simplex, seborrheic keratosis, pigmented actinic keratosis, and lentigo maligna [8]. Features of the pigmented lesions on the face differ from the lesions on the other parts of the body. Novel dermoscopic criteria are identified for the facial lesions [9].

In this study, we aimed to determine the correlation between dermoscopic and histopathological findings in the diagnosis of hyperpigmented flat facial lesions.

Materials and methods

The patients who presented to the Dermatology Department of Cukurova University School of Medicine with flat hyperpigmented lesions, such as facial solar lentigo, seborrheic keratosis, and actinic keratosis were included in the study. Based on the history, clinical evaluation, Wood's lamp examination, and dermoscopic evaluation, the patients with diseases that form hyperpigmentation on the face such as melasma, nevus of Ota, nevus spilus, ephelis, Cafe au lait spots, drug eruption, postinflammatory hyperpigmentation, photosensitive dermatitis, verruca plana, tinea versicolor, actinic lichen planus were excluded. Participants' names, ages, and skin phenotypes based on Fitzpatrick's classification were recorded. The study was conducted with the approval of the Ethics Committee of Clinical Research of Cukurova University (approval number: 2006/10-1).

A dermoscopy device (MoleMax II, DermaInstruments, Vienna Austria), which can magnify the lesions 30 times, was used during the dermoscopic evaluation. The pictures of the lesions were recorded in JPEG format in 640x480 pixels and 24bit color. Evaluations were made by two researchers at the same time and the findings were recorded on a form of dermoscopic diagnostic criteria, prepared for solar lentigo, seborrheic keratosis, actinic keratosis, and lentigo maligna.

The dermoscopic diagnostic criteria of solar lentigo, seborrheic keratosis, actinic keratosis, and lentigo maligna were deduced from the Color Atlas of Dermatoscopy [10], An Atlas of Surface Microscopy of Pigmented Skin Lesions [5], Color Atlas of Melanocytic Lesions of the Skin [11], and the studies of Stolz et al. [12], Pock et al. [13], Peris et al. [14], Stante et al. [15], Zalaudek et al. [16], Braun et al. [17], Schiffner et al. [18], Robinson JK [19], Cognetta et al. [20] and Elgart et al. [21] were used as the references. Since the references classified the diagnostic criteria of actinic keratosis as non-pigmented and pigmented, our cases were also categorized accordingly.

The patients signed the consent forms before the skin biopsy, and photographs of the lesions were taken. The biopsy samples were sent to Cukurova University Pathology Department for histopathological evaluation.

Statistical analysis

Statistical analysis of the numerical variables was performed using SPSS (Statistical Package for the Social Sciences) 16 software (IBM Corporation, Armonk, New York, US). Frequencies and percentages were calculated for demographic parameters. *P*-values of less than 0.05 indicated significance. Statistical analysis was performed with the Kappa test. A score between 0-0.40 indicates weak consistency, 0.40-0.75 indicates moderate consistency and 0.75-1.0 indicates excellent consistency in the Kappa test [22].

Results

A total of 53 skin lesions of 51 patients (26 males (51%) and 25 females (49%)) were evaluated in the study. The mean age of the patients was 64.47 (11.24) years (range: 40-83 years). Type II skin phenotype was present in 30 patients, and type III phenotype was present in the rest (n=21). Histopathological evaluation revealed the following diagnoses: Seborrheic keratosis in 9, actinic keratosis in 32, solar lentigo in 9, actinic keratosis plus solar lentigo in 3 patients. These findings were summarized in Table 1. Most patients had multiple lesions. Dermatological examination revealed various symptoms of photoaging such as atrophy, wrinkles, and telangiectasia surrounding the lesions.

The most common dermoscopic finding was whiteyellow squama (n=25, 47%) on the flat hyperpigmented lesions on the face. The rest of the findings included annular-granular pattern (n=22, 41%), pink-to-red pseudo-network (n=18, 34%), brown-to-gray segmented pseudo-network structure (n=18, 34%) and moth-eaten border (n=17, 32%).

Table 1: General Information of the patients included in the study

Patients	Age	Gender	Skin phenotype	Dermoscopic diagnosis	Histopathological diagnosis
Patient 1	54	М	3	SK	SK
Patient 2	60	М	2	AK	AK
Patient 3	42	Μ	3	AK	AK
Patient 4	73	М	2	AK	AK
Patient 5	65	Μ	2	AK	SK
Patient 6	77	М	3	SL	AK
Patient 7	64	F	2	SL	AK + SL
Patient 8	63	М	2	SK	SL
Patient 9	50	F	2	AK	AK
Patient 10	62	F	2	AK	AK
Patient 11	77	F	2	AK	AK
Patient 12	78	Μ	2	SL	AK + SL
Patient 13	49	F	2	SK	SK
Patient 14	77	Μ	2	SL	SL
Patient 15	83	Μ	2	AK	SK
Patient 16	58	Μ	2	AK	AK
Patient 17	65	Μ	2	SK	AK
Patient 18	76	F	2	AK	AK
Patient 19	57	Μ	3	SL	SL
Patient 20	67	F	2	AK	AK
Patient 21	72	Μ	2	SK	SK
Patient 22	50	F	3	AK	AK
Patient 23	44	F	3	AK	AK
Patient 24	40	F	3	AK	AK
Patient 25	73	F	3	SL	SL
Patient 26	60	F	3	AK	AK
Patient 27	64	Μ	2	AK	AK
Patient 28	77	Μ	2	AK	SK
Patient 29	71	F	2	AK	AK
Patient 30	80	М	2	SK	SK
Patient 31	80	М	2	SL	SL
Patient 32	80	М	2	AK	AK
Patient 33	69	М	3	AK	AK
Patient 34	79	М	2	AK	AK
Patient 35	70	М	3	SL	SL
Patient 36	57	F	2	AK	AK
Patient 37	60	F	2	SL	SL
Patient 38	80	F	2	AK	SL
Patient 39	61	F	2	AK	AK
Patient 40	45	F	2	SL	AK
Patient 41	65	M	2	AK	AK + SL
Patient 42	57	M	3	AK	SL
Patient 43	42	F	3	AK	AK
Patient 44	65	F	3	AK	AK
Patient 45	64	F	2	AK	AK
Patient 46	67	F	2	AK	AK
Patient 47	62	M	3	AK	AK
Patient 48 Patient 40	69 71	F F	3	AK AK	AK
Patient 49	71		3		AK
Patient 50	80	M F	3	AK	AK
Patient 51 Patient 52	67 76		3	SK	SK
Patient 52 Patient 53	76 54	M M	3 3	SK AK	SK AK
Diagnoses a	ire		diagnoses is	Diagnoses a	are incompatible
compatible		compatible			

SK: Seborrheic Keratosis, AK: Actinic Keratosis, SL: Solar Lentigo

The most common dermoscopic findings of the solar lentigo patients were moth-eaten border and jelly sign (Figure 1), of the seborrheic keratosis patients, sharp border and sudden cessation of pigmentation, moth-eaten border, and jelly sign (Figure 2), and in patients with actinic keratosis, white-yellow squama, brown-to-gray segmented pseudo-network structure, annular-granular pattern and pink-to-red pseudo-network (Figure 3). These findings were summarized in Table 2.

Figure 1: Moth-eaten edge and jelly sign. Dermoscopically and histopathologically diagnosed with solar lentigo



Figure 2: Brain-like appearance and white-yellow scale. Dermoscopically and histopathologically diagnosed with seborrheic keratosis

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Figure 3: White-yellow scales, brown-gray patchy pseudo-meshwork, dark brown or black follicular openings showing asymmetric pigmentation. Dermoscopically and histopathologically diagnosed with actinic keratosis



Table 2: Evaluation of the patients according to the dermoscopic diagnostic criteria

Diagnosis	Dermoscopic Diagnostic Criteria	Number of positive lesions	Percentage of positive lesions
Solar Lentigo	Homogeneous color	0	0
	Moth-eaten border	7	78
	Jelly sign	6	66
	Fingerprint pattern	0	0
	Thin, brown pseudo-network	0	0
Seborrheic	Milia-like cysts	0	0
Keratosis	Comedone-like openings	0	0
	Fissures and ridges (brain-like appearance)	2	22
	Moth-eaten border	4	44
	Jelly sign	4	44
	Fingerprint pattern	0	0
	Sharp border and sudden cessation of pigmentation	5	55
	Hairpin vessels	0	0
Non-pigmented	a-Pink-to-red pseudo-network	15	47
Actinic Keratosis	b-White-yellow squama	18	56
	c-Linear-wavy vessels surrounding the hair follicle	11	34
	d-White halo around the hair follicle with yellowish keratotic plug	11	34
	Strawberry view (a+b+c+d)	5	15
	Non-specific pattern-yellow color (if hyperkeratosis is evident)	2	6
Pigmented Actinic Keratosis	Lead blue or dark brown spots and globules surrounding the follicle orifices	11	34
	Annular-granular pattern	16	50
	Rhomboidal structure	0	0
	Brown-to-gray segmented pseudo- network	17	53

Three patients whose lesions were histopathologically diagnosed with actinic keratosis plus solar lentigo were excluded from statistical evaluation. The dermoscopic preliminary diagnosis and the histopathological final diagnosis were inconsistent in 9 (18%) lesions. The histopathological diagnosis of 6 out of 9 lesions was confirmed as seborrheic keratosis with dermoscopy, and 3 lesions were diagnosed with actinic keratosis. Likewise, among actinic keratosis lesions (n=32), the preliminary dermoscopic diagnoses matched the histopathological results in 29 lesions; two lesions were assessed as solar lentigo and 1 lesion was classified as seborrheic keratosis with dermoscopy. Six out of 9 lesions with histopathological solar lentigo diagnosis were assessed as solar

lentigo, 2 as actinic keratosis, and 1 as seborrheic keratosis by dermoscopy (Table 3).

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Table 3: Dermoscopic-histopathological diagnosis of the patients

	Seborrheic Keratosis	Histopatholog Actinic Keratosis	ical Solar Lentigo	Total
Dermoscopic				
Seborrheic	6	1	1	8
Keratosis				
Actinic Keratosis	3	29	2	34
Solar Lentigo	0	2	6	8
Total	9	32	9	50

The Kappa test result was 0.645 (*P*<0.001). Dermoscopic and histopathological diagnoses were moderately compatible in flat hyperpigmented facial lesions.

Discussion

Facial diseases can cause pigmentation either during the natural course of the disease or secondarily. Although some of these diseases are easily diagnosed due to non-facial localization and their specific clinical features, differential diagnosis can be difficult in solar lentigo, seborrheic keratosis, actinic keratosis, and lentigo maligna [23]. To resolve this issue, dermoscopy can be used in combination with clinical examination.

Facial lesions demonstrate special features in dermoscopic evaluation. Since the rete ridges in this area are flat, a conventional pigment network and the arising features cannot be found. Pseudo-network appearance can be observed during dermoscopic examination. Pseudo-network is an irregular network resulting from the puncture of the dark-colored skin surface by the hair follicles or sweat glands, or the combination of adjacent follicles surrounded by a hyperpigmented area. This structure can be seen in facial lesions such as solar lentigo, seborrheic keratosis, actinic keratosis, lentigo maligna and lentigo maligna melanoma [10, 13, 24].

It is quite difficult and sometimes even impossible to clinically differ the facial lentigo maligna from solar lentigo, seborrheic keratosis, and actinic keratosis. Furthermore, a single lesion can demonstrate the dermoscopic elements of seborrheic keratosis, actinic keratosis, and lentigo maligna at the same time. Even though dermoscopy is an important method in the differential diagnosis of facial lesions, histopathological evaluation still should be made to establish the final diagnosis of suspicious lesions [14, 25].

Stante et al. [15] clinically diagnosed solar lentigo in 4 cases with pigmented facial lesions. However, during the dermoscopic examination, these lesions were suspected to be lentigo maligna and the histopathological evaluation confirmed this diagnosis. This study emphasized that the early stage lentigo maligna, which could not be detected with clinical examination, could be accurately diagnosed with the use of dermoscopy.

Dermoscopic features of facial pigmented actinic keratosis include a large number of lead blue or dark brown spots and globules surrounding the follicle orifices. Histopathologically corresponding to this appearance is melaninloaded macrophages in the upper dermis. An annular-granular pattern is formed with the conjugation of these spots and globules in time. Brown-to-gray segmented pseudo-network was suggested as a dermoscopic criterion in recent years [14].

The most common dermoscopic findings in the cases that were histopathologically diagnosed with actinic keratosis

were as follows: White-yellow squama (18 lesions, 56%), brown-to-gray segmented pseudo-network (17 lesions, 53%), annular-granular pattern (16 lesions, 50%), pink-to-red pseudo-network (15 lesions, 47%), linear-wavy vessels surrounding the hair follicle (11 lesions, 34%), a white halo around the hair follicle with yellowish keratotic plug (11 lesions, 34%), lead blue or dark brown spots and globules surrounding the follicular orifice (11 lesions, 34%).

Nascimento et al. [26] emphasized the importance of an inner gray halo in distinguishing pigmented actinic keratosis from lentigo maligna dermoscopically. This manifestation was defined as a white halo around the hair follicle with a yellowish keratotic plug in our study and detected in 11 lesions (34%).

Akay et al. [27] reported that pigmented actinic keratosis has clinical and dermoscopic features similar to lentigo maligna. Therefore, they emphasized that histopathological examination is still the gold standard for accurate diagnosis.

In two patients with facial actinic keratosis, Zalaudek et al. [25] reported two patterns, which are specific for lentigo maligna: Annular-granular pattern involving asymmetric pigmented follicles, numerous small gray-brown spots surrounding the hair follicles, and brown-to-gray rhomboidal structure. Additionally, moth-eaten border and jelly sign, frequently seen in seborrheic keratosis and solar lentigo, were observed in these two patients.

In patients who were histopathologically diagnosed with actinic keratosis, dermoscopic findings were consistent with lentigo maligna: Short dark brown or black streaks in 7 (22%) and dark brown or black asymmetric pigmented follicular orifices in 3 (9%). Likewise, shared findings of seborrheic keratosis and solar lentigo, such as a moth-eaten border and jelly sign were seen in five (16%) and three (9%) lesions, respectively.

Seborrheic keratosis is usually diagnosed with clinical examination. However, in some cases, especially in the diagnosis of pigmented seborrheic keratosis, the following dermoscopic diagnostic criteria have significance: Milia-like cysts, comedone-like openings, structures similar to the brain sulci and gyri (cerebriform pattern), moth-eaten border, jelly sign, fingerprint pattern, sharp demarcation and hairpin vessels [10, 17, 28]. Among them, comedone-like openings and milia-like cysts are the most common [17, 29].

Braun et al. [17] identified 15 dermoscopic criteria in the study, which evaluated the dermoscopic findings of 203 patients with pigmented seborrheic keratosis for the presence of the above-mentioned criteria. They observed hairpin vessels in 63%, a sharp demarcation in 90%, comedone-like openings in 71%, milia-like cysts in 66%, fissures in 61%, and moth-eaten border in 46% of the lesions. The researchers noted that the majority of the lesions were papulonodular and plaque-type.

Lesions histopathologically diagnosed as seborrheic keratosis had the following dermoscopic findings in our study: A sharp demarcation and sudden cessation of pigmentation (in 5 lesions, 55%), moth-eaten border (in 4 lesions, 44%), jelly sign (in 4 lesions, 44%) and cerebriform pattern (in 2 lesions, 22%). Other dermoscopic findings consistent with actinic keratosis, such as a white-yellow squama was seen in 4 (44%) lesions, and a white halo surrounding the hair follicle with yellowish

keratotic plug, a pink-to-red pseudo-network, and the annulargranular pattern was observed in 2 (22%) lesions. The most common dermoscopic findings of seborrheic keratosis, such as comedone-like openings and milia-like cysts, were not observed since the lesions in our study were flat-surfaced.

The fingerprint pattern is a dermoscopic finding of seborrheic keratosis and solar lentigo. This pattern, described by Schiffner et al. [30] comprises light brown, delicate, and parallel arranged fingerprint-like structures. Braun et al. [17] noted the fingerprint pattern in 10% of the seborrheic keratosis lesions.

In our study, none of the seborrheic keratosis and solar lentigo lesions had the fingerprint pattern. The most common dermoscopic findings were moth-eaten border (n=7, 78%) and jelly sign (n=6, 67%) in cases that were histopathologically diagnosed as solar lentigo. Also, dermoscopic findings consistent with actinic keratosis, including lead blue or dark brown spots and globules surrounding the follicular orifices, and annulargranular pattern were demonstrated in 2 (22%) lesions.

In our study, no patient was diagnosed with lentigo maligna dermoscopically or histopathologically. In a multicenter retrospective study, Tiodorovic-Zivkovic et al. [31] reported that gray color is the most important dermoscopic criterion in the diagnosis of lentigo maligna.

Lallas et al. [32] emphasized that white and prominent follicular openings, squamous and red color in dermoscopy are important diagnostic clues to distinguish pigmented actinic keratosis from lentigo maligna; however, intense pigmentation and gray rhomboidal lines suggest lentigo malignancy.

Sahin et al. [9] compared the dermoscopic findings of facial pigmented lesions including solar lentigo, seborrheic keratosis, lentigo maligna, and lentigo maligna melanoma. In this study, they emphasized that milia-like cysts, pseudo-follicular openings, the cerebriform pattern, light brown globules, and light brown and yellow-opaque homogenous areas were the most common dermoscopic criteria of the benign pigmented skin lesions.

In our study, the most common dermoscopic finding in the flat hyperpigmented facial lesions was white-yellow squama (n=25, 47%). The rest of the findings were an annular-granular pattern (n=22, 41%), a pink-to-red pseudo-network (n=18, 34%), a brown-to-gray segmented pseudo-network (n=18, 34%) and a moth-eaten border (n=17, 32%).

In a meta-analysis, Bafounta et al. [33] assessed 8 studies and compared the diagnostic ratio of clinical evaluations and dermoscopic findings. They found that the diagnostic specificity and sensitivity of dermoscopy were higher. On the other hand, the use of dermoscopy still does not provide a 100% accurate diagnosis and it never substitutes histopathological evaluation.

Costa-Silva et al. [34] reported that dermoscopy increases the diagnostic accuracy of flat pigmented facial lesions; however, histopathological evaluation is the gold standard for accurate diagnosis.

Dermoscopy had a sensitivity and specificity of 66.7% and 95.1%, respectively, in seborrheic keratosis, 90.6%, and 72.2%, respectively, in actinic keratosis and 66.7%, and 95.1%, respectively, in solar lentigo. These findings are consistent with the studies in the literature. In the light of the previous and the

present study findings, we can state that dermoscopic examination contributes to a more accurate diagnosis of pigmented lesions.

In a study comparing the dermoscopic and histopathological diagnoses in nevi, Sahin et al. [35] found the two methods well compatible. In ours, the two were moderately consistent.

The coexistence of two different types of neoplasms is called a collision tumor. These types of lesions are relatively rare. Collision lesions located on the face usually show an atypical morphology. These lesions cause difficulties in differential diagnosis [36]. In this study, three lesions histopathologically diagnosed as actinic keratosis plus solar lentigo were excluded.

Limitations

The most important limitation of our study was the small number of patients. Secondly, the number of patients with solar lentigo, seborrheic keratosis, and actinic keratosis differed. Also, none of our patients had lentigo maligna.

Conclusion

We observed a moderate agreement between dermoscopic examination and histopathological evaluation. One should not be contented with the clinical examination of the pigmented lesions on the face; if possible, a dermoscopic examination should also be performed for a more accurate diagnosis. The use of new dermoscopic criteria to be determined over time will support a more accurate diagnosis. Since a dermoscopic diagnosis of facial pigmented lesions cannot be based on the presence of a single criterion, we can deduce that histopathological examination is still the gold standard for accurate diagnosis.

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