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Dermatoscopy of Facial Non-Pigmented Actinic Keratosis and Intraepidermal Carcinoma

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Abstract

Dermatoscopy improves the diagnostic accuracy of non-pigmented facial lesions, including actinic keratosis (AK) and intraepidermal carcinoma (IEC) and helps to differentiate them from common invasive malignancies such as basal cell carcinoma and invasive squamous cell carcinoma. The most common dermatoscopic features characterizing AK are background erythema/erythematous pseudonetwork, white follicular openings/targetoid hair follicles, surface scales, rosettes, fine, linear, wavy vessels, microerosions and sun-damaged surrounding skin. In comparison, the most common dermatoscopic features of IEC are background erythema, red starburst pattern, surface scale, dotted/glomerular vessels, hairpin vessels, microerosions/ulcerations and targetoid hair follicles. The practice of recognizing these features in dermatoscopic images is a useful tool in the armamentarium of a clinician examining skin lesions.

Keywords: actinic keratosis, erythematous facial lesions, squamous cell carcinoma in situ, bowenoid actinic keratosis

1. Introduction

Actinic keratosis (AK) and other forms of squamous cell carcinoma (SCC) in situ are among the most common lesions in dermatological practice and are primarily the result of cumulative UV damage. The clinical relevance of accurate diagnosis relies on several factors. Firstly, misdiagnosing an inflammatory disease as an AK would lead to unnecessary and possibly harmful usage of destructive therapies on benign lesions. Secondly, AK is commonly a lesion in a field of sun-damaged skin, and among other lesions associated with chronic sun damage, some small clinically indistinguishable carcinomas may rest. Moreover, AK, although a common lesion, might progress to invasive SCC with gradual changes that can be visualized under a dermatoscope [1]. Furthermore, studies have shown that most SCCs arise from or in close proximity to AK and that dermatoscopy aids in differentiation between AK and SCC [2, 3]. Therefore, dermatoscopy is a useful tool for a clinician examining non-pigmented facial lesions allowing to differentiate between them.

Several forms of in situ SCC that are united by atypical keratinocytes in the epidermis but vary clinically, dermatoscopically, and histopathologically have been recognized [4]. Actinic keratosis (AK) and intraepidermal carcinoma (IEC) are the two main types of SCC in situ affecting facial skin. Much less common forms

include arsenical keratosis, radiation keratosis (caused by ionizing radiation), and hydrocarbon keratosis, in which dermatoscopic differences have not been described [5]. The following chapter will provide an overview of the clinical and dermatoscopic features that characterize different forms of AK and IEC of the face, including the dermatoscopic progression model from AK to invasive SCC.

2. Definition of actinic keratosis and intraepidermal carcinoma

The differentiation between AK and IEC relies on their histopathologic characteristics.

AK is also called solar or senile keratosis, SCC in situ AK-type, or keratinocytic intraepidermal neoplasia and represents a common lesion on chronically sun-damaged skin of fair skinned individuals. Histopathologically, AK presents as atypia of basal keratinocytes with loss of polarization, crowding, and overlapping that can extend up to near full thickness atypia in advanced lesions [5–8].

IEC is an intraepithelial SCC exhibiting full-thickness cellular dysplasia [9]. However, other synonyms employed for extragenital full-thickness intraepidermal carcinoma are Bowen's disease, in situ SCC, cutaneous SCC in situ, and intraepithelial SCC [1]. It is noteworthy that in comparison with other types of SCC in situ, Bowen's disease has been defined as SCC in situ arising on sun-protected skin, without field damage and possibly without association with HPV, although previously suggested otherwise [10–12]. For the consistency of this chapter, the term "*intraepidermal carcinoma*" will be used to describe facial intraepithelial SCC exhibiting full-thickness cellular dysplasia.

3. Diagnosing AK and IEC

Actinic keratosis in the majority of cases can be diagnosed clinically. Nevertheless, the clinical description of an erythematous macule or patch with a superficial scale may correspond to many other skin lesions and dermatoses. Studies [13, 14] examining the diagnostic precision of clinically diagnosed AK have reported misdiagnosis rates of approximately 10%. The main biopsy diagnoses in cases of misdiagnosis were SCC in situ, SCC with superficial invasion, seborrheic keratosis, basal cell carcinoma, and other benign skin lesions and dermatoses such as subacute spongiotic dermatitis, rosacea, solar elastosis, scars and verrucae plana. Pivotal differential diagnosis of AK is invasive SCC that can mimic AK if presenting as an erythematous macule. It has been shown that 1.5% of clinically diagnosed AK lesions identified by board-certified dermatologist were SCCs with superficial invasion on histologic assessment [13]. In comparison, dermatoscopy improves the diagnostic accuracy of both AK and SCC. A recent systematic review and study by Huerta-Brogeras *et al.* showed sensitivity up to 98.7% and specificity up to 95% if AK is diagnosed with dermatoscopy [15, 16].

Diagnosis of IEC is based on clinical, dermatoscopic, and histopathologic features.

3.1 Clinical features of AK and IEC

The most frequent presentation of both AK and IEC is a variably erythematous scaly patch or slightly elevated plaque [17]. AK is either single or multiple, while IEC is usually a single lesion. In comparison with AK, IEC is often an indurated

lesion on palpation. Both lesions are asymptomatic in most of the cases, although some patients experience discomfort, such as burning, pain, bleeding, and pruritus [6]. It has been noted that pain can be equally present in both AK and IEC, but is more common in invasive SCC [18].

A broad and useful tool for clinical description of the thickness of AK is a classification by Olsen *et al.* [19]. In this classification:

- Grade 1 AKs are mild - slightly palpable, better felt than seen.
- Grade 2 AKs are moderately thick that are easily seen and felt.
- Grade 3 AKs are severe - very thick, hyperkeratotic, and obvious AK.

However, this clinical classification cannot reliably predict the histological grade proposed by Roewert-Huber *et al.* that could justify the classical progression model of AK to invasive SCC through clinical thickening and histopathological upward extension of atypical keratinocytes before invasion. It has been shown that only 26% of Olsen grade 1 lesions were grade 1 on histopathology with atypical keratinocytes in the basal and suprabasal layers of the epidermis, 75% of Olsen grade 2 lesions were grade II on histopathology with atypical keratinocytes extending to the lower two-thirds of the epidermis and only 14% of Olsen grade 3 lesions had corresponding grade III on histopathology with atypical keratinocytes extending to more than two thirds of the full thickness of the epidermis [8, 20].

3.2 Dermatoscopic features of AK and IEC

For the description of dermatoscopic features of AK and IEC, both metaphoric and descriptive language can be used. Definitions of the main metaphoric and descriptive terms are given in **Table 1**.

Main dermatoscopic features of AK are depicted in **Table 2**. Main dermatoscopic features of IEC are depicted in **Table 3**.

Metaphoric/descriptive terms	Definition
Red pseudonetwork	Marked pink-to-red background erythema surrounding accentuated hair follicles
Red starburst pattern	Radially arranged structureless red lines or hairpin vessels that surround a yellow to white structureless scaly center and that resemble an overall starburst appearance
Rosettes	Four bright white dots or clods arranged together as a square (or 4-leaf clover)
Shiny white streaks	Short discrete white lines oriented parallel and orthogonal (perpendicular) to each other seen only under polarized dermatoscopy
Strawberry pattern	Red pseudonetwork in combination with targetoid hair follicles
Targetoid hair follicle	Yellowish keratotic plug within a prominent hair follicle opening surrounded by a white halo
White circles	Bright white circles surrounding an orange/yellow keratin plug

Table 1.
 Standardized terms of common dermatoscopic features for AK and IEC [18, 21–23] .

Classic AK	Most common dermatoscopic findings	
	• Background erythema/erythematous pseudonetwork	Strawberry pattern
	• Follicular openings/ targetoid hair follicles	
	• Surface scales	
	○ Yellow-white opaque scales	
	○ Diffuse/discrete scales	
	• Rosettes	
	• Fine, linear, wavy vessels	
	• Microerosions	
	• Sun damaged surrounding skin	
	Less common, but possible findings	Structure is more characteristic to
	• Central scale	IEC, SCC, KA
	• Dotted/glomerular vessels	IEC
	• White structureless areas (common in Korean patients)	SCC, KA
	A rare finding	Structure is more characteristic to
	• Central ulceration	SCC, KA
	• Linear-irregular vessels	KA, SCC
	• Hairpin vessels	SCC, KA, IEC
	• Red starburst pattern	IEC, SCC
	• Shiny white streaks	Dermatofibroma, scar, BCC
Bowenoid AK	Most common dermatoscopic findings	
	• Glomerular vessels regularly distributed	
	• Surface scale	
Hyperkeratotic AK	Most common dermatoscopic findings	
	• Marked hyperkeratosis seen as white-yellow structureless areas preventing visualization of underlying structures	

Table 2.

Dermatoscopic features of AK categorized in three groups according to their prevalence. The most common dermatoscopic findings – Features present in almost all to the majority of AKs. Less common, but possible findings – Present in some AKs, although more common and characteristic for other lesions. A rare finding – Sometimes present in AK, but a differential diagnosis is much more likely. Abbreviations: AK – Actinic keratosis; IEC – Intraepidermal carcinoma; KA - Keratoacanthoma; SCC – Squamous cell carcinoma; BCC – Basal cell carcinoma [1, 6, 15, 22–26].

3.2.1 Characteristics of specific features

3.2.1.1 Erythematous pseudonetwork

Erythematous pseudonetwork can be defined as a marked pink-to-red background erythema formed by fine wavy telangiectatic vessels surrounding accentuated hair follicles [23]. It is one of the most common and characteristic findings of AK.

IEC	Most common dermatoscopic findings	
	<ul style="list-style-type: none"> • Background erythema • Red starburst pattern • Surface scales <ul style="list-style-type: none"> ○ Yellow-white opaque scales ○ Central scale ○ Diffuse/discrete scales • Dotted/glomerular vessels • Hairpin vessels • Microerosions/ulcerations • Targetoid hair follicles 	
	Less common, but possible findings	Structure is more characteristic to
	<ul style="list-style-type: none"> • Rosettes 	
	<ul style="list-style-type: none"> • Central keratin mass 	KA, SCC
	<ul style="list-style-type: none"> • Red pseudonetwork 	AK
	A rare finding	Structure is more characteristic to
	<ul style="list-style-type: none"> • White structureless areas 	KA, SCC
	<ul style="list-style-type: none"> • Linear-irregular vessels 	KA, SCC
	<ul style="list-style-type: none"> • Central ulceration 	BCC, SCC, KA

Table 3. *Dermatoscopic features of IEC categorized in three groups according to their prevalence. The most common dermatoscopic findings – Features present in almost all to majority of IECs. Less common, but possible findings – Present in some IECs, although more common and characteristic for other lesions. A rare finding – Sometimes present in IEC, but a differential diagnosis is much more likely. Abbreviations: AK – Actinic keratosis; IEC – Intraepidermal carcinoma; KA – Keratoacanthoma; SCC – Squamous cell carcinoma; BCC – Basal cell carcinoma [1].*

3.2.1.2 Targetoid hair follicles

Targetoid hair follicles are formed by yellowish keratotic plugs within the hair follicles and surrounded by a whitish halo. This feature is particularly common for AK on the nose and hyperkeratotic AK [23].

3.2.1.3 Strawberry pattern

Strawberry pattern (**Figure 1**) is a composite appearance of reddish pseudonetwork and hair follicles. This pattern is present in up to 95% of AK [23].

3.2.1.4 Surface scales

Scales are one of the most common features of AK and correlate with hyperkeratosis and parakeratosis on histopathology [21]. The distribution is usually diffuse throughout the lesion, although some lesions can be partly scaly (**Figure 1**) and a central scale is common for hyperkeratotic lesions. The color of the scales varies from white to yellow and an accumulation of exogenous pigment has been reported [27].

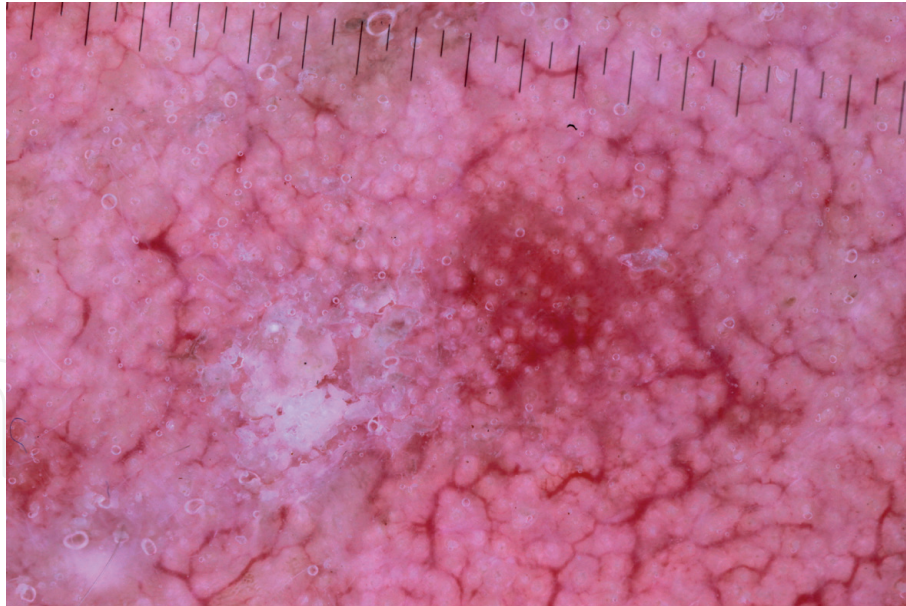


Figure 1. Dermatoscopic image of an AK. White scales limiting visualization of the underlying structures are seen on the left side of the picture, while a typical strawberry pattern with erythematous pseudonetwork and targetoid hair follicles are seen on the right side.

3.2.1.5 Rosettes

Rosettes are also named 4-dotted-clods in descriptive terminology. Rosettes are a clue for keratinizing neoplasms, although they can also be observed in several other conditions including basal cell carcinoma, melanoma, melanocytic nevus, dermatofibroma, scar, molluscum contagiosum, actinically damaged skin and cicatricial alopecia of lichen planopilaris [28]. The dermatopathological correlate of 4-dotted-clods in AK is horizontally arranged alternating hyperkeratotic and parakeratotic corneal layers in the follicular infundibula associated with mild peri-follicular fibrosis [28]. It has also been proposed that smaller 4-dotted-clods are caused by the concentric horn in the follicle at the infundibular level, whereas larger ones are caused by concentric fibrosis around the follicle [29].

3.2.1.6 Fine, linear, wavy vessels

Focused linear wavy vessels surrounding the hair follicles was found in more than 80% of facial AKs in a study by Zalaudek *et al.* These peculiar linear, wavy vessels of facial AK clearly differ in morphology from the arborizing vessels of vessels of nodular basal, short fine telangiectatic vessels of superficial basal cell carcinoma, and regular hairpin vessels that are characteristic of seborrhoeic keratosis. Furthermore, wavy vessels typically encircle the hair follicles as single and uniform units, which contrasts with the irregularly sized and distributed linear irregular vessels that can be seen in amelanotic/hypomelanotic melanoma, areas of regression in melanoma, or invasive SCC [23].

3.2.1.7 Microerosions

Microerosions are small erosions on the surface of the lesion seen under a dermatoscope. Microerosions are twice as common in IEC in comparison with AK, but are also a common feature of superficial basal cell carcinoma [1].

3.2.1.8 Shiny white streaks

Shiny white streaks (SWS) are also known as chrysalis or crystalline structures by their metaphoric terms. Dermatoscopically, SWS are only visible in a polarized light dermatoscopy as white, perpendicular, few millimeters long lines. Histopathologically, SWS are caused by polarization of thickened hyaline fibrous bundles and therefore considered as a dermatoscopic sign of dermal fibrosis. Shiny white streaks have been reported in a variety of skin lesions, mainly dermatofibromas, scars, basal cell carcinomas, lichen planus like keratosis, invasive melanoma, melanoma metastasis and sometimes even solar lentigo and intradermal nevus. In addition, it has been reported that SWS might be less common in inflamed lesions [22, 25, 29–31].

3.2.1.9 Sun damaged surrounding skin

The importance of recognizing the features of the surrounding skin is based on several factors. First of all, AK quite commonly has a confluent solar lentigo on the border. Secondly, it has been hypothesized that humans focus on the lesion and not on the surrounding skin and therefore are outperformed by artificial intelligence in the precision of AK diagnosis. Moreover, teaching medical students to pay attention to chronic sun damage in the background improved the frequency of correct diagnoses of pigmented actinic keratoses from 32.5% to 47.3% [26]. In addition, lesions arising in field cancerization have a higher potential for malignant progression. The latter has been recognized in a new nomenclature of keratinocyte cancers by Conforti *et al.* According to the authors, all keratinocyte cancers should be classified in two groups - 'cSCC+field' for keratinocyte cancers arising in the presence of AK within the field of cancerization and 'cSCC-field' for keratinocyte cancers arising in the absence of AK or field cancerization [32].

3.2.1.10 Red starburst pattern

Red starburst pattern can be defined as radially arranged structureless red lines or hairpin vessels that surround a yellow to white structureless scaly center and that resemble an overall starburst appearance (**Figure 2**). Red starburst pattern is equally common in IEC and invasive SCC, and less common in AK [1].

3.2.1.11 Dotted/glomerular vessels

Dotted vessels are tiny red dots densely aligned next to each other [1]. Glomerular vessels are larger-caliber reddish dots formed by tortuous capillaries curled up into a ball and resembling the glomerular apparatus of the kidneys. Glomerular vessels are specific for Bowen's disease, if located in clusters and bowenoid AK, if distributed regularly. Glomerular vessels can also be present in stasis dermatitis, psoriasis, irritated seborrheic keratosis, superficial basal cell carcinoma and melanoma [33–35]. The combination of clustered dotted/glomerular vessels and hyperkeratosis has been previously shown to achieve a 98% diagnostic probability for IEC [1, 35].

3.2.1.12 Hairpin vessels

Hairpin vessels are vessels that double back on themselves and are seen as loops when they are oblique to the surface of the lesion. Hairpin vessels are a common feature of keratinizing tumors and are a hallmark of seborrheic keratosis in which

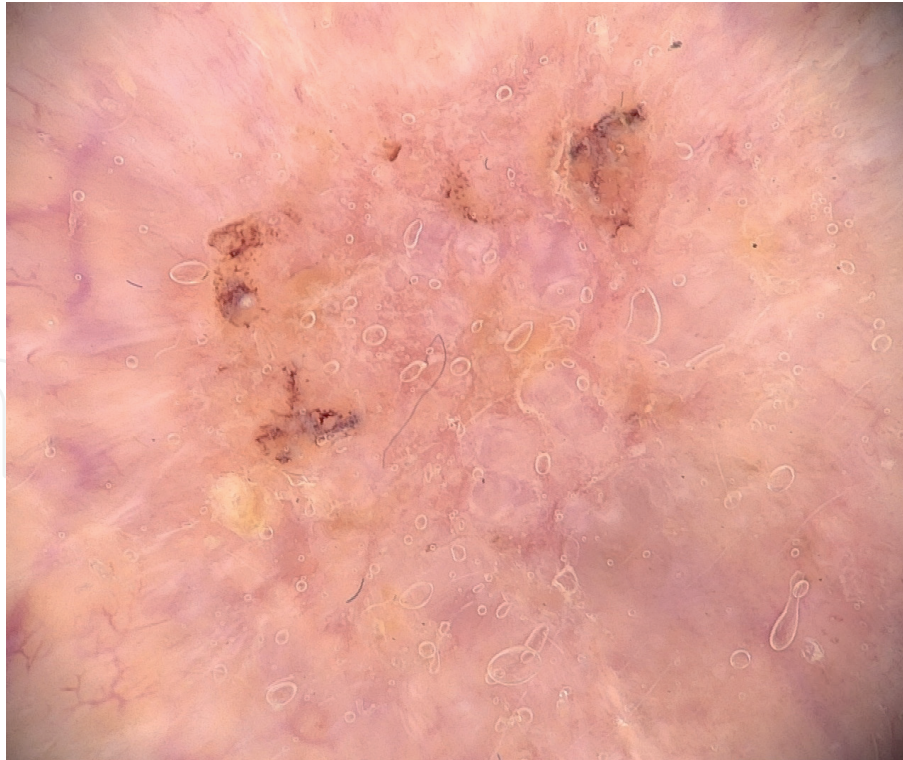


Figure 2.
Dermatoscopic image of IEC presenting with red starburst appearance formed by red and white radially arranged lines and central pink structureless clods, yellow scales, and hemorrhagic crusts.

they are usually regularly distributed and surrounded by a white halo. Hairpin vessels are a rare but possible finding in AK and a common finding in IEC and SCC. Hairpin vessels are associated with progression of IEC to invasive SCC and clinically thicker lesions. Positive predictive value of hairpin vessels for seborrheic keratosis is 70%, contrasting with only 13.3% for squamous cell carcinoma [1, 33].

3.2.2 Variants of AK

Apart from classical AK, other forms categorized histopathologically are hypertrophic, atrophic, bowenoid, acantholytic, pigmented, lichenoid, and proliferative variants, although in this grading system overlap of histologic subtypes may occur in a single lesion [36].

Atrophic AK. In this form, the lesion has an atrophic epidermis on histopathology [5]. According to one study, atrophic type AK more commonly presents with red pseudonetwork [37].

Bowenoid AK has a characteristic dermatoscopic feature of glomerular vessels regularly distributed along the lesion (**Figures 3 and 4**), thus differentiating it from Bowen's disease, whose vessels are irregularly distributed and grouped [6].

Hyperkeratotic AK presents with a nonspecific dermatoscopic pattern due to hyperkeratosis, which prevents visualization of the underlying structures [6]. In addition, it has been shown that the surface keratin of AK can accumulate exogenous pigmentation, particularly from broad spectrum sunscreens containing titanium dioxide. Such a specific feature of bright arctic-blue or greenish-blue color of AK on polarized light dermatoscopy has been described and named an "iceberg sign" [27].

Lichenoid AK clinically presents with pronounced erythema around the base of the lesion secondary to an underlying lichenoid infiltrate on histopathology [5]. Dermatoscopically, lichenoid AK might also present with a more intense erythematous background.



Figure 3.
Dermatoscopic image of bowenoid AK. Dermatoscopically regularly distributed glomerular (upper left) and hairpin (right and lower part) vessels in addition to a central white scale are seen.

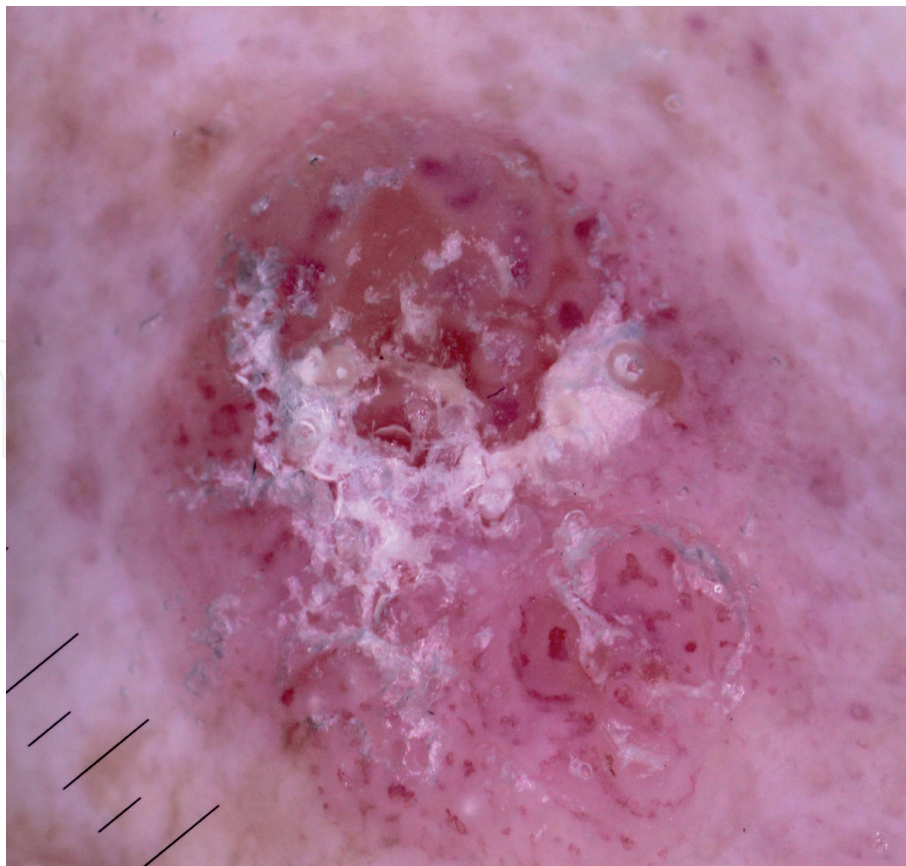


Figure 4.
Dermatoscopic image of bowenoid AK. Dermatoscopically regularly distributed dotted and glomerular vessels, white surface scales, yellow clods corresponding to hyperkeratosis (upper part), and few milium like cysts (lower left fragment) are seen.

3.2.3 Dermatoscopic–histopathologic correlations of AK

Skilled observers can predict the histologic grade of AK with dermatoscopy, although in consensus with clinical features some studies do not find such correlations [37, 38]. The following dermatoscopic–histopathologic correlations have been previously proposed:

- Grade 1 AK on dermatoscopy is typified by a red pseudonetwork and discrete white scales; this pattern correlates with grade I on histopathology where the keratinocytic atypia is mild and limited to the basal and suprabasal layers of the epidermis.
- Grade 2 AK is dermatoscopically characterized by an erythematous background intermingled with white to yellow, keratotic, and enlarged follicular openings. This described pattern in dermatoscopy resembles the surface of a strawberry, therefore was originally termed a strawberry pattern. In grade 2 AK, the histopathological changes are diffuse, with the lower two-thirds of the epidermis involved by atypical keratinocytes with alternating orthokeratosis and parakeratosis on the surface.
- Grade 3 AKs dermatoscopically exhibit either enlarged follicular openings filled with keratotic plugs over a scaly and white-yellow-appearing background or marked hyperkeratosis seen as white-yellow structureless areas. This grade on dermatoscopy corresponds to full-thickness atypia with increased mitotic activity and hyperkeratosis/parakeratosis [39].

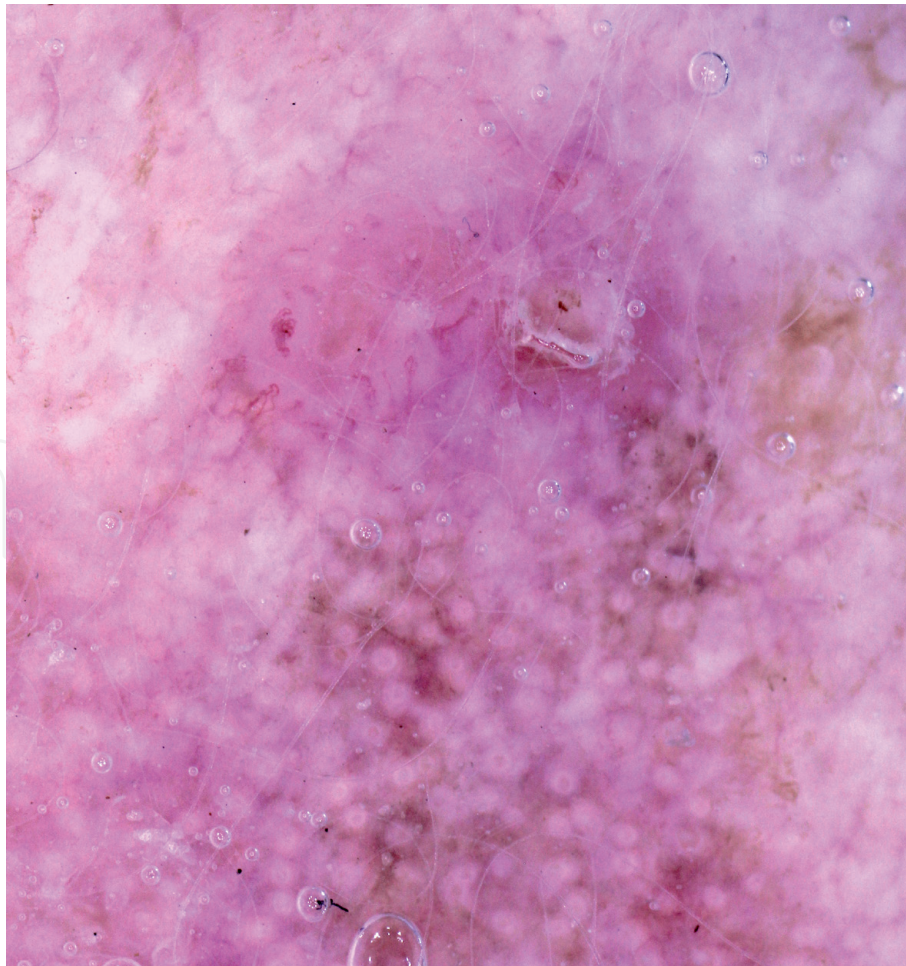


Figure 5. *Histopathologically confirmed basosquamous carcinoma on the border of an AK. Dermatoscopically, two coalescent nodules, both with central ulceration and crust and peripheral dotted and hairpin vessels with white surrounding halo can be seen.*

3.3 Dermatoscopic features of AK progressing to SCC

Progression from AK to SCC might follow two pathways. The classical multistep pathway requires proliferation of atypical keratinocytes upwards through the entire epidermis and accumulation of further mutational and cellular events that lead to invasive growth [40]. Nevertheless, the differentiated pathway assumes that invasive SCC may directly arise from a proliferation of atypical basaloid cells of the epidermal basal layer without full-thickness atypia [41].

Dermatoscopic features suggesting progression of AK towards SCC are dotted/glomerular vessels, hairpin vessels, white halos surrounding vessels, ulceration/bleeding, white structureless areas, and white circles surrounding follicles [24]. Appearance of these additional dermatoscopic features is an important clue to perform a diagnostic biopsy even in long-standing AKs, as a great majority of SCCs are associated with preexisting AKs [3] (**Figure 5**).

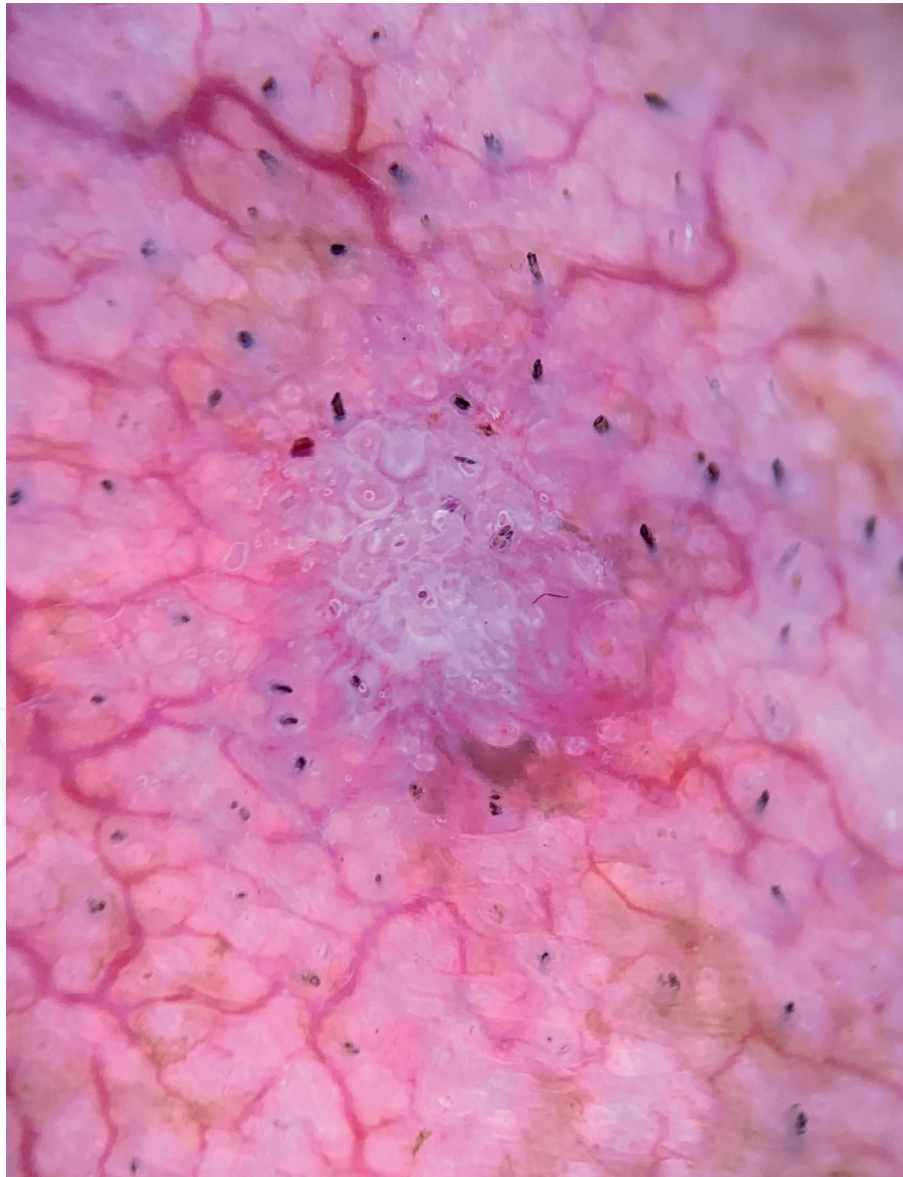


Figure 6.

A lesion on the lower part of the left cheek that clinically presented as an erythematous indurated papule 5 mm in diameter. Dermatoscopically white circles (throughout the lesion), white structureless area (lower part), rosettes (in periphery), and dotted vessels (on the lower part) can be seen. Histopathologically, the basal growth pattern showed filiform papillary elongation protruding into the upper dermal structures in length that exceeds the overlying epidermis.

3.3.1 Characteristics of specific features

3.3.1.1 White circles

On the basis of dermatoscopic–histopathologic correlation, white circles correspond to acanthosis and hypergranulosis of the infundibular epidermis or hyperkeratosis of the infundibular epidermis associated with central keratin plugs [28, 42].

White circles (**Figure 6**) are a specific feature of SCCs and keratoacanthoma-like SCC (KA) and have been shown to be equally common in both and more frequently than in other raised nonpigmented lesions. Moreover, when SCC and KA-like SCC were contrasted with AK and Bowen's disease, the positive predictive value of white circles was 92% in favor of SCC and KA-like SCC [42]. Nevertheless, another study did not find a statistically significant difference between the prevalence of white circles in KA-like SCC and SCC, vs., AK and BD [28]. Other lesions with white circles described are basal cell carcinomas, Bowen's disease, seborrheic keratosis, lichen planus–like keratosis, lichen simplex chronicus, folliculitis, ulcer, chondrodermatitis nodularis helioides, and a dermal nevus [42].

4. Conclusion

Dermatoscopy is a useful tool for the differentiation of AK, IEC, and other non-pigmented facial lesions. The diagnosis is based on the combination of lesion specific factors such as background and follicular structures, vascular patterns, and surface characteristics in addition to information received from the surrounding skin.

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