Dermatology Practical & Conceptual

Cutaneous Squamous Cell Carcinoma: Clinico-Dermoscopic and Histological Correlation: About 72 Cases

Sara El-Ammari[1], Sara Elloudi[1], Hanane Baybay[1], Meryem Soughi[1], Zakia Douhi[1], Fatima Zahra Mernissi[1], Mohammed Omari[2], Samira El fakir [2], Layla Tahiri[3]

1 Department of Dermatology, University Hospital Hassan II, Faculty of Medicine and Pharmacy, Sidi Mohamed Ben Abdellah University, Fez, Morocco

2 Laboratory of Epidemiology, Clinical Research and Community Health- Faculty of Medicine and Pharmacy, Sidi Mohamed Ben Abdellah University, Fez, Morocco

3 Anatomical pathology laboratory, University Hospital Hassan II, Faculty of Medicine and Pharmacy, Sidi Mohamed Ben Abdellah University, Fez, Morocco

Key words: cutaneous squamous cell carcinoma, dermoscopy, histopathological grade of differentiation, clinical form

Citation: El-Ammari S, Elloudi S, Baybay H, et al. Cutaneous Squamous Cell Carcinoma: Clinico-Dermoscopic and Histological Correlation: About 72 Cases. *Dermatol Pract Concept*. 2024;14(1):e2024042. DOI: https://doi.org/10.5826/dpc.1401a42

Accepted: September 24, 2023; **Published:** January 2024

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

Corresponding Author: Dr El-Ammari Sara, Department of Dermatology, University Hospital Hassan II, Fes, Morocco. Phone Number: +212 616820719 Email: saraelammari2@gmail.com

ABSTRACT

Introduction: Cutaneous squamous cell carcinoma (cSCC) is the second most common skin cancer, accounting for 20% of malignant skin tumors. Dermoscopy is a very useful tool for diagnosing cSCC, and its findings are confirmed through histopathological studies.

Objectives: to describe the different dermoscopic structures of invasive cSCC and investigate their association with the clinical form and histopathological grade of differentiation.

Methods: We conducted a cross-sectional study, collecting all patients diagnosed with squamous cell carcinoma over a period of 5 years. The study population was divided into two groups based on histological differentiation (well-differentiated and non-well-differentiated) and clinical form (nodulo-ulcerative and nodular). Various dermoscopic parameters were compared between these groups.

Results: Out of 72 invasive cSCC, 81.9% were well-differentiated, while 18.1% were non-well- differentiated. The clinical form of cSCC was nodulo-ulcerative in 83.3% of cases and nodular in 16.7%. Well-differentiated tumors showed dotted, glomerular and hairpin vessels, along with a predominant white pattern characterized by centrally distributed keratin as well as white circles, and whitish perivascular halo ($P < 0.05$). The distribution of these white structures was radial in nodulo-ulcerarive

lesions, whereas in nodular lesions, their distribution, as well as that of keratin, was more diffuse ($P < 0.05$). Non-well-differentiated tumors showed a combined white-red pattern with the predominance of arborizing vessels ($P < 0.05$).

Conclusions: Our results show the reliability of dermoscopy as a tool for distinguishing between well- and poorly differentiated cSCC. This distinction is characterized by an increase in predominantly arborizing vessels and a corresponding decrease in white structures as the tumor progresses from a well-differentiated to a poorly differentiated state. Additionally, the nodulo-ulcerative form exhibits a central distribution of keratin, while the nodular form displays a diffuse distribution.

Introduction

Cutaneous squamous cell carcinoma (cSCC) is the second most common skin cancer after basal cell carcinoma [1,2]. It may occur de novo or as a result of precursor lesions [1]. cSCC accounts for 20% of malignant cutaneous tumors, and its incidence is steadily rising due to population aging and increased emphasis on skin cancer screening [2-4]. Dermoscopy has become one of the fundamental diagnostic techniques in clinical practice, that allows in vivo evaluation of skin colors and microstructures [5]. The majority of dermoscopic structures, including white, vascular and pigmented structures have direct histopathologic correlations, making this technique a useful means of communication between pathologists and clinicians [6]. The degree of histopathological differentiation in cSCC ranges from good to moderate or poor, serving as a significant prognostic factor [7]. Poor differentiation is an independent risk factor for metastasis, recurrence, and disease-specific mortality, while well-differentiated SCC is associated with a five-year recurrence-free survival rate of 83% [8]. Thus, early and aggressive management of high-risk cSCC, including poorly differentiated tumors, is recommended to reduce morbidity and mortality [8]. However, while the dermoscopic criteria of cSCC have been well described, there remains a paucity of research examining the correlation between the histopathological grade of differentiation. Previous studies have reported that the white pattern predominates in well-differentiated cSCC, while the red pattern is more prevalent in poorly differentiated cSCC. Additionally, there is a scarcity of studies investigating the correlation between clinical form and dermoscopic features [7].

Objectives

The aim of this study was to describe the different dermoscopic structures of invasive cSCC and investigate their association with clinical form and histopathological grade of differentiation.

Methods

This is a cross-sectional study performed in the dermatology department of HASSAN II University Hospital, Faculty of Medicine and Pharmacy, Sidi Mohamed Ben Abdellah University of Fez, Morocco. The study extended over a period of 5 years, from November 2017 to July 2022.

The inclusion criteria consisted of patients with skin lesions that were histopathologically confirmed as invasive cSCC. Exclusion criteria included patients with poor quality dermoscopic images, lesions histologically proven to be keratoacanthoma or SCC in situ and patients with xeroderma pigmentosum.

Dermoscopic images were captured with a Dermlite DL4 ‘4Gen, at a magnification of 10×, using both polarized and non-polarized light, with and without immersion. Two investigators evaluated the dermoscopic images of all selected lesions according to predefined criteria [5-10] and which are presented in Table 1. Additionally, it states that the evaluators were blinded to the histology of the lesion when assessing the dermoscopic features of each lesion.

The dermatoscopic evaluation was based on pattern and color analysis, including vessel morphology density and distribution, as well as the presence or absence of different white structures such as scales, keratin, white circles, white structureless areas, white perivascular halos, chrysalis and rosettes. The distribution of these structures and the accuracy of the predominant pattern (red, white or combined white- red pattern) and the presence of other structures like erosions, ulceration and Hemorrhage were also assessed.

The recruited cases underwent total excision or biopsy and were submitted to routine histopathological confirmation using hematoxylin and eosin staining.

In this study, cSCC was categorized into two grades of histological differentiation: well and non-well differentiated. Moderately and poorly differentiated cSCC were evaluated together, due to the small number of cases. The clinical forms were classified as nodular and nodulo-ulcerative lesions.

Table 1. Definitions of the criteria used in the evaluation of dermoscopic images.

Dermoscopic criteria	Definition
Vascular structures	
Dotted vessels	Tiny red dots, usually densely distributed next to each other
Glomerular vessels	They are usually larger than the dotted vascular structures, they are tortuous capillaries often distributed in clusters mimicking the glomerular apparatus of the kidney
Hairpin vessels	Vascular loops sometimes twisted and bending
Linear irregular vessels	Linear or slightly curved, irregularly shaped vascular structures
Linear regular vessels	Linear vascular structures no branches or curves
Comma vessels	Coarse vessels that are slightly curved and barely branched
Arborizing vessels	Vessels of large diameter that branch irregularly into finest terminal capillaries
Polymorphous vasculature	The presence of at least two of the morphological types of vessels described above
Vessel quantity (> or < 50%)	Vascular structures detected in more or less than half of the lesion surface
Vessel distribution (radial, diffuse)	Arrangement of vascular structures all over the lesion or at the periphery
White structures	
Scales/keratin	White or yellow areas lying on the surface, without any recognizable structure
Keratin distribution (central, diffuse)	Arrangement of keratin in the center or all over the lesion
White circles	Roundish structures composed of yellow to light-brown structureless center and white outer structureless rim
Whitish structureless areas	Whitish areas not corresponding to scales/keratin, in the absence of any recognizable structure
Chrysalis	white shiny linear streaks that are seen under polarized dermoscopy. It does not encompass blotches and strands.
Rosettes	Four closely aggregated white, small dots in correspondence to follicular opening and resembling 4-leaf clover
Peri-vascular whitish halo	White rim surrounding vascular structures
white structures distribution	Arrangement of white structures all over the lesion, at the periphery or in the center
Ulceration	Large irregularly shaped or roundish areas of dull red or red-brown structureless color
Erosions	Small and irregularly distributed orange to red to red-brown structureless areas; they correspond to superficial hemorrhages and are usually associated with yellow opaque structures
Hemorrhage	Blood clearly visible in areas covering more than 10% of the lesion surface
Predominant pattern (white, red or combination)	The color observed in more than 50% of the lesion surface. Combination refers to the presence of white and red color in almost equal parts of the lesion surface

Statistical Analysis

The data were analyzed using version 26.0 of SPSS for Windows. The mean ± standard deviations for numerical variables and the number and % values for categorical variables were given as descriptive statistics. Comparative dermoscopic analysis between the different dermoscopic parameters among the two histological subgroups and the clinical forms were performed by chi-square test or Fisher exact test depending on the sample size of the parameter to compare. For multivariate analysis, binary logistic regression was used. Values of P less than 0.05 were accepted as significant.

Results

Patients Demographics, Clinical Characteristics and Dermatopathological Findings

Of 160 histologically confirmed cSCC cases, 88 were excluded due to uninterpretable dermoscopic images. A total of 72 cSCC were collected of which 49 were male (68.1%) and 23 were females (31.9%), the mean age at diagnosis was 68.67 years with extremes (25- 1). Concerning the origin 46 of our patients (63.9%) came from an urban environment, while 26 (36.1%) from a rural environment. Chronic sun

exposure was reported in 49 patients (68.1%) and 5 patients had a history of skin cancer (6.9%). Based on the origin of lesions, 54 (75%) lesions were de novo; 7 patients (9.7%) had developed cSCC on a burn scar, 6 (8.3%) on a chronic wound, 4 (5.6%) on a lichen and in one patient (1.4%) on hereditary epidermal bullosa. Associated actinic keratosis lesions diagnosed through clinical examination and dermoscopy were found in 16 patients (22.2%). In our series 57 patients (79.2%) consulted at the tumor stage, while the remaining patients consulted at an earlier stage. Clinically, 49 patients had a phototype IV (68.1%) and 20 had a phototype III (27.8%). The frequency distribution of the lesions across various sites was as follows: cervicocephalic extremity (N = 32; 44.4%), lower limbs (N = 26; 36.1%), oral mucosa (N = 7; 9.7%), genital mucosa (N = 4, 5.6%) and upper limbs (N = 3; 4.2%). The clinical form of cSCC was nodulo-ulcerative in 60 patients (83.3%) and nodular in 12 patients (16.7%). The mean size of the lesions was 6.52 cm. According to the histopathological grade of differentiation, 59% or 81.9% of the cSCC lesions were well differentiated and 13% or 18.1% were non-well differentiated.

Dermatoscopic Analysis

The analysis of different dermoscopic structures in SCC, according to the clinical form and histopathological grade of differentiation in our series, is presented in Tables 2, 3, 4 and 5.

Correlation Dermoscopy-Histopathological Differentiation Grade (Tables 2 and 3)

The most observed dermoscopic aspects in well-differentiated cSCC (figure1) were: dotted vessels (N = 44 ,74.6%), glomerular (N = 36 ,61%), hairpin (N = 44, 74.6%), whitish scales (N = 44, 74.6%), yellowish scales (N = 51 ,86.4%), keratin (N = 56, 94.9%) with central distribution (N = 39, 69.6%), white circles (N = 44, 74.6%), whitish structureless areas (N = 49, 83.1%), perivascular whitish halo (N = 41, 69.5%) with a predominance of the white pattern (N = 38, 64.4%) and < 50% of vascular structures. All these dermoscopic aspects were significantly correlated with well-differentiated cSCC (P < 0.05).

For non-well differentiated cSCC (Figures 2 and 3), arborizing vessels were the most common dermoscopic feature (N = 9; 69.3%) and was associated with a higher risk of developing non well differentiated squamous cell carcinoma OR = 14.8 [2.43; 90.37]. The other dermoscopic features that exhibited a statistically significant difference in non-well differentiated SCC included a vessel quantity higher than 50% (N = 9; 69.3%) with a predominance of the combined white-red pattern (N = 8, 61.5%).

Linear irregular vessels, vascular polymorphism, rosettes, chrysalis, presence of ulceration and hemorrhagic spots were present in both well- and non-well-differentiated groups with comparable percentages (Table 2) without statistically significant difference (P > 0.05)

Correlation Dermoscopy-Clinical Form (Tables 4 and 5)

The most observed dermoscopic aspects in nodulo-ulcerative variant (Figure 4) were: opaque yellowish scales (N = 52; 86.7%), hemorrhagic spots (N = 54; 90.0%), the presence of ulceration (N = 60; 100% OR = 0.015 [0.001; 0.178]), the central distribution of keratin N = 39; 72.2% OR = 11.120 [1.184; 104.483]) and the radial distribution of different white structures with a predominance of the white pattern (N = 36; 60%). All these dermoscopic aspects showed a statistically significant correlation with the nodulo-ulcerative form, with a Pvalue < 0.05. Other aspects were also predominant in this form, but the correlation was statistically non-significant, such as hairpin vessels (N = 42; 70%), whitish structureless areas (N = 47; 78.3%) and peri-vascular whitish halo (N = 41; 68.3%).

Concerning the nodular form (Figure 3), the distribution of keratin and different white structures was diffuse, with percentages of (N = 7; 70.0%) and (N = 9; 75.0%) respectively, with the predominance of the white-red pattern, being statistically significant (P < 0.05) for each feature. However, the presence of comma vessels, arborizing vessels and regular linear vessels was more present in this form, with percentages of 33.3%, 50.0% and 25.0% respectively. However, the P value for these features was > 0.05, indicating a non-significant correlation.

Conclusions

The incidence of cutaneous squamous cell carcinoma (cSCC) has been increasing worldwide for several decades and is estimated to be 15 to 35/100,000 people per year [2]. It is more common in males than in women and affects the older population (80% of cases are in adults over 60), due to the correlation with cumulative sun exposure [3]. The epidemiological characteristics of the patients in our study are consistent with previous data.

Invasive cSCC can develop de novo, or from pre-cancerous lesion or certain chronic inflammatory skin areas, such as chronic wounds, burns, scars, ulcers etc [3,4], as was the case in some of our patients.

Dermoscopy is an essential in-vivo, non-invasive diagnostic method that provides the visualization of morphological characteristics not detectable with the naked eye [11]. Only a limited number of studies have been conducted primarily focusing on the correlation between degree of differentiation and dermoscopy.

In this study, we identified useful clues that may suggest the degree of differentiation of cSCC. The presence of

Table 2. Comparison of dermoscopic aspects according to histopathological differentiation grade.

DERMOSCOPIC STRUCTURES	DIFFERENTIATION GRADE		
	Well differentiated N = 59	Non-well differentiated N = 13	P-value
Vascular structures			
Dotted vessels	44 (74.6%)	5 (38.5%)	.016
Glomerular vessels	36 (61%)	3 (23.1%)	.014
Hairpin vessels	44 (74.6%)	5 (38.5%)	.016
Comma vessels	9 (15.3%)	4 (30.8%)	.176
Linear irregular vessel	50 (84.7%)	11 (84.6%)	.637
Linear regular vessel	8 (13.8%)	0 (0.0%)	0.180
Arborizing vessels	11 (18.6%)	9 (69.3%)	.001
Polymorphous vasculature	54 (91.5%)	12 (92.3%)	.705
Quantity of vessels			.004
<50%	44 (74.6%)	4 (30.8%)	
>50%	15 (25.4%)	9 (69.3%)	
Vessels distribution			.448
Radial	19(32.2%)	5 (38.5%)	
Diffuse	40 (67.8%)	8 (61.5%)	
White structures			
Whitish scales	44 (74.6%)	5 (38.5%)	.016
Opaque yellow scales	51 (86.4%)	7 (53.8%)	.015
Keratin	56 (94.9%)	8 (61.5%)	.004
Keratin distribution			.045
Central	39(69.6%)	3 (37.5%)	
Diffuse	17 (30.4%)	5 (62.5%)	
White circles	44 (74.6%)	4 (30.8%)	.004
Whitish structureless areas	49 (83.1%)	5 (38.5%)	.002
Chrysalis	21 (35.6%)	4 (30.8%)	.505
Rosettes	26 (44.1%)	6 (46.2%)	.565
Peri-vascular whitish halo	41 (69.5%)	5 (38.5%)	.039
White structures distribution			.327
Central	6 (10.2%)	1 (7.7%)	
Radial	30 (50.8%)	4 (30.8%)	
Diffuse	23 (39.0%)	8 (61.5%)	
Erosion	0 (0%)	1 (7.7%)	.181
Ulceration	51 (86.4%)	12 (92.3%)	.486
Hemorrhage	52(88.1%)	9 (69.2%)	.103
Predominant pattern			.022
White	38 (64.4%)	3 (23.1%)	
Red	3 (5.1%)	2 (15.4%)	
White and red	18 (30.5%)	8 (61.5%)	

previously described white structures, including scales, centrally distributed keratin, white circles, perivascular whitish halo and whitish structureless areas were strongly associated with well-differentiated cSCC, while the diffuse distribution of keratin and other white structures were more likely to be present in non-well-differentiated cSCC. This finding aligns with the results reported by Saleh HM et al, Lallas et al, and Zalaudek et al reported that these whitish structures were associated with well- or moderately differentiated variants and that a central distribution of scales or keratin was associated

with a 36-fold reduced possibility for poor differentiation [7,8,12]. In the latter, signs of keratinization are not found [8,12,13], while the moderately differentiated variant would show less expression of dermoscopic white indices compared to the well differentiated cSCC [7].

The vascular findings observed in our analysis of well-differentiated tumors are characterized by dotted, glomerular, and hairpin vessels, with the presence of a whitish perivascular halo. In contrast, non-well differentiated tumors exhibited predominantly branched or arborizing vessels. These findings are consistent with the results of Pyne et al [14], who also demonstrated through their study that non-well differentiated tumors tended to be histologically deeper than well differentiated lesions. This deeper invasion may account for the higher prevalence of linear and branching vessels, which are more commonly observed as tumors increase in thickness and contribute to tumor development.

Our results are not in agreement with those of Saleh et al [7], who documented that well-differentiated lesions had a higher incidence of linear irregular vessels followed by glomerular vessels and hairpin vessels. According to Lallas et al [13], well-differentiated cSCC is characterized by elongated peripheral vessels reminiscent of the arborescent vessels of basal cell carcinoma, while poorly differentiated cSCC shows a polymorphic vascularization. Similar observations were made by Zalaudek [12] in poorly differentiated squamous cell carcinoma, where a reddish background accompanied small-caliber linear vessels, hairpin vessels, or glomerular vessels. In contrast, the well-differentiated subtype primarily exhibited hairpin and dot vessels.

We found that the quantity of vessels was significantly correlated with the degree of differentiation, which is consistent with the results of Lallas et al [8]. They reported that tumors with over 50% of the lesion area covered by vessels had a 30- to 120-fold higher possibility of being poorly differentiated. They also added that vessel caliber was also found to be a significant predictor of degree of differentiation, since

Table 3. Results of the multivariate analysis of the correlation between dermoscopic features and histological differentiation grade.

	Odds ratio	Confidence interval 95%
Arborizing vessels	14.8	[2.43; 90.37]
White circles	.033	[0.003; 0.356]
Whitish structureless areas	.031	[0.003; 0.331]

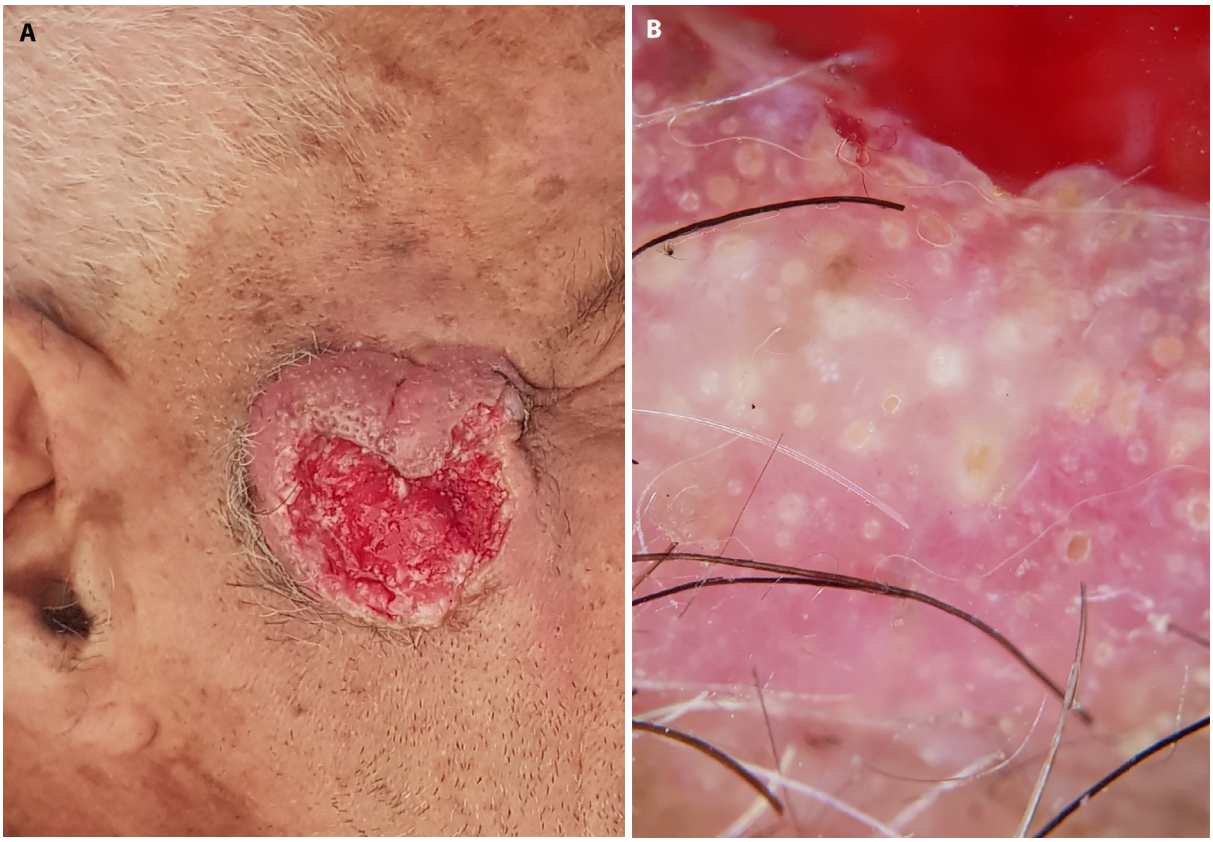

Figure 1. A) Nodulo-ulcerative well-differentiated squamous cell carcinoma located in the cheek. (B) Dermoscopy reveals a predominantly white pattern, white circles, rosettes, whitish structureless areas, dotted and glomerular vessels with <50% of vascular structures, ulceration.

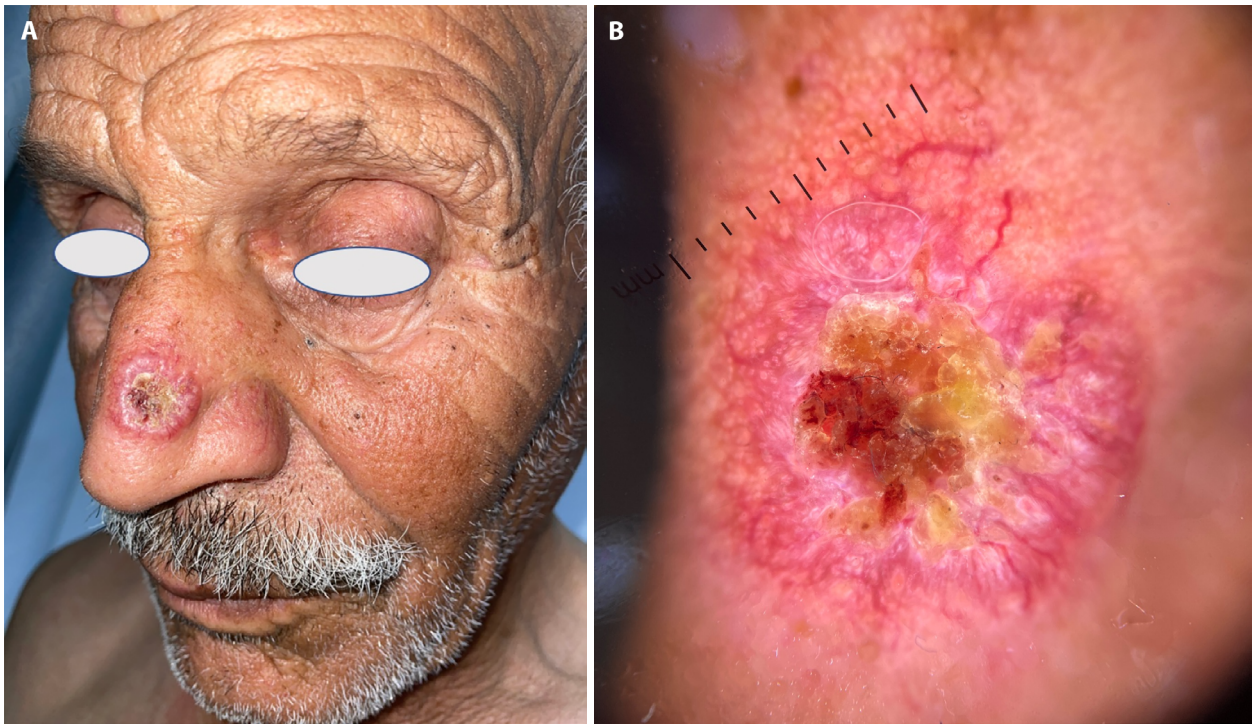

Figure 2. (A) Moderately differentiated nodule ulcerative tumor of the nose. (B) Dermoscopy shows a combined white-red pattern, rosettes, chrysalis, keratin, hemorrhage, arborescent and linear irregular vessels radially arranged.

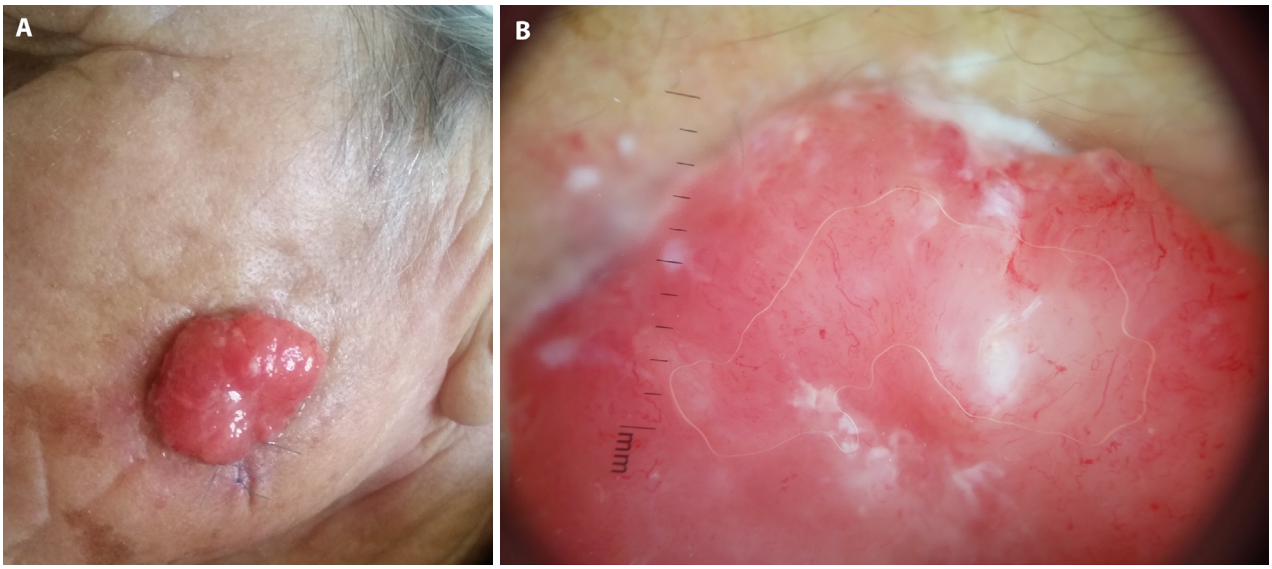

Figure 3. (A) Poorly differentiated Nodular tumor of the cheek. (B) Dermoscopy shows a red pattern, polymorphic vasculature diffusely distributed over > 50% of the tumor surface, made of arborescent, linear irregular vessels and comma vessels, whitish structureless areas, whitish scales with diffuse distribution.

a small caliber vessel had a threefold higher probability of poor differentiation while those with large caliber vessels had an 83% lower probabilities of being poorly differentiated [8]. Lallas et al also revealed that the presence of a predominantly red color, attributed to the absence of desquamation and keratin and the presence of bleeding and/or dense vasculature, was in favor of poor differentiation, while a predominantly white or white-yellow color reduced the probability of a poorly differentiated cSCC [8]. These results are consistent with ours and those of Saleh et al [7].

Concerning the correlation of dermoscopic aspects and the clinical form, to the best of our knowledge, only one study has investigated this correlation. This gap in the literature motivated our research, as we aim to contribute significantly to the field. Saleh et al [7] examined 17 lesions representing three clinical forms of cSCC: nodular,

Table 4. Comparison of dermoscopic aspects according to clinical form.

DERMOSCOPIC STRUCTURES	CLINICAL FORM		
	Nodulo-ulcerative N = 60	Nodular N = 12	P-value
Vascular structures			
Dotted vessels	41 (68.3%)	8 (66.7%)	.578
Glomerular vessels	33 (55.0%)	6 (50%)	.498
Hairpin vessels	42 (70.0%)	7 (58.3%)	.318
Comma vessels	9 (15.0%)	4(33.3%)	.137
Linear irregular vessel	51(85.0%)	10 (83.3%)	.587
Linear regular vessel	5(8.5%)	3(25.0%)	.127
Arborizing vessels	14(23.3%)	6(50.0%)	.067
Polymorphous vasculature	55 (91.7%)	11(91.7%)	.680
Quantity of vessels			.157
<50%	42(70.0%)	6 (50.0%)	
>50%	18(30.0%)	6 (50.0%)	
Vessels distribution			.378
Radial	21 (35.0%)	3(25.0%)	
Diffuse	39 (65.0%)	9(75.0%)	
White structures			
Whitish scales	42(70.0%)	7(58.3%)	.318
Opaque yellow scales	52 (86.7%)	6(50.0%)	.009
Keratin	54 (90.0%)	10(83.3%)	.399
Keratin distribution			.015
Central	39 (72.2%)	3 (30.0%)	
Diffuse	15 (27.8%)	7(70.0%)	
White circles	39 (65.0%)	9 (75.0%)	.378
Whitish structureless areas	47(78.3%)	7(58.3%)	.138
Chrysalis	20(33.3%)	5(41.7%)	.404
Rosettes	27 (45.0%)	5 (41.7%)	.545
Peri-vascular whitish halo	41 (68.3%)	5 (41.7%)	.079
White structures distribution			.043
Central	6 (10%)	1 (8.3%)	
Radial	32(53.3%)	2(16.7%)	
Diffuse	22(36.7%)	9 (75.0%)	
Erosion	1(1.7%)	0(0.0%)	.833
Ulceration	60 (100%)	0(0%)	.000
Hemorrhage	54 (90.0%)	7(58.3%)	.015
Predominant pattern			.025
White	36 (60.0%)	4 (33.3%)	
Red	2 (3.3%)	3 (25.0%)	
White and red	22 (36.7%)	5(41.7%)	

nodulo-ulcerative, and ulcerative. They found that nodular and nodulo-ulcerative lesions showed mainly linear irregular vessels followed by glomerular vessels. In ulcerative lesions, glomerular vessels dominated, with a vessel quantity greater than 50% for nodulo-ulcerative and ulcerative tumors and less than 50% for the nodular form. In our study, linear irregular vessels were the most frequently observed, followed by dotted vessels and then glomerular vessels in both studied forms, Additionally, we found a higher presence of hairpin vessels in the nodulo-ulcerative form and an increased

occurrence of arborescent vessels in the nodular form, with a vessel quantity less than 50% in the nodulo-ulcerative tumors, contrary to the above results. For whitish structures, whitish perivascular halo and whitish structureless areas were present in both forms, but more found in the nodulo-ulcerative form. Nodular lesions exhibited a dominant presence of white circles, along with a diffuse distribution of keratin. In contrast, the nodulo-ulcerative form showed a central distribution of keratin. These results were not consistent with those of Saleh et al [7], who detected a central distribution of keratin in both nodular and nodulo-ulcerative forms, the presence of white circles in all nodular lesions and in more nodulo-ulcerative than ulcerative lesions with the absence of perivascular whitish halo in the latter form and its presence in the other two forms.

In the same study [7], they concluded that nodular and nodulo-ulcerative lesions were significantly associated with well-differentiated cSCC, whereas ulcerative lesions were significantly associated with moderately differentiated cSCC. This association between clinical form and degree of differentiation was not investigated in our study.

Table 5. Results of the multivariate analysis of the correlation between dermoscopic features and clinical form.

	Odds ratio	Confidence interval 95%
Keratin distribution	11.120	[1.184; 104.483]
ulceration	0.015	[0.001; 0.178]

The main limitation of our study is the combined analysis of non-well-differentiated tumors, which was due to the small number of poorly differentiated (N = 3) and moderately differentiated (N = 10) cSCC. In addition, the dermoscopic images were interpreted retrospectively, which introduces a potential bias. However, it is important to emphasize that we applied rigorous criteria in the selection process, excluding any images of poor quality. As a result, the number of cases included in the analysis was reduced.

Our study highlights the potential of dermoscopy as a non-invasive technique to provide clinicians with valuable insights into the histopathological differentiation of SCC. In addition, our study emphasizes the importance of collaboration between clinicians and anatomopathologists when an immunohistochemical complement is required, particularly in cases of poorly differentiated tumor proliferation. By engaging in discussions and considering immunohistochemical markers specific to poorly differentiated squamous cell carcinomas, particularly when a dermoscopic red pattern with a predominance of arborizing vessels is visualized. This collaborative approach not only improves patient care but also carries economic benefits by optimizing the selection and utilization of immunohistochemical resources.

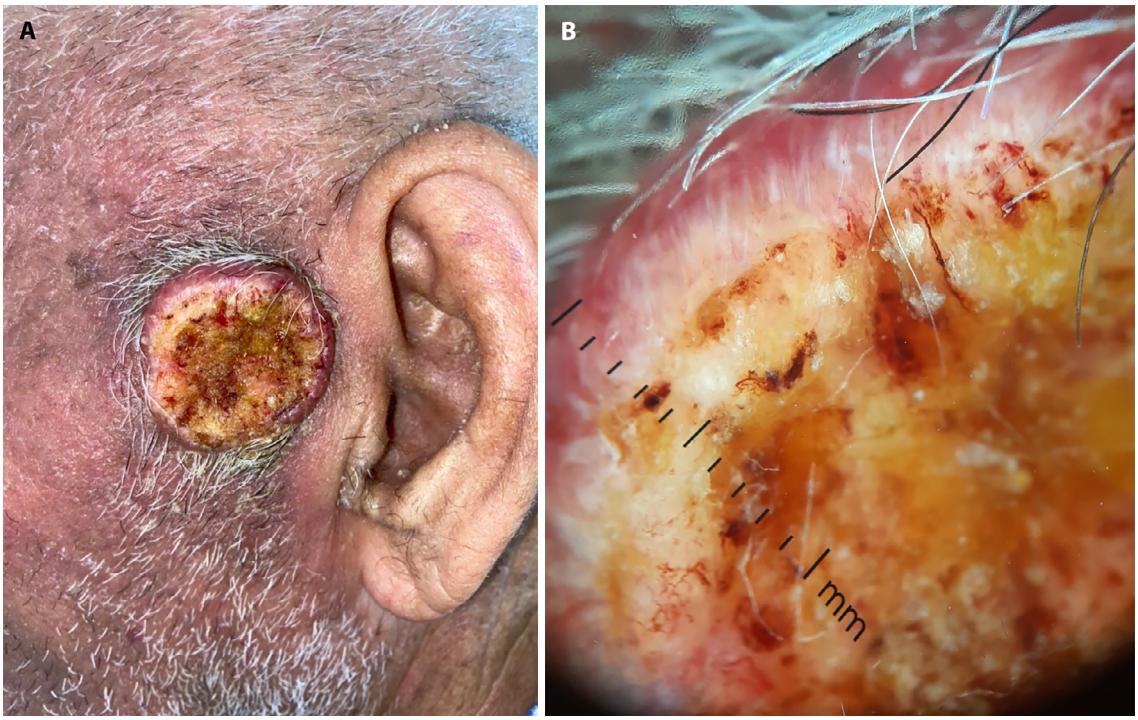

Figure 4. (A) Nodulo-ulcerative Well-differentiated squamous cell carcinoma located in the cheek. (B) Dermoscopy reveals a predominantly white pattern, central mass of keratin, whitish scales, chrysalis, radial arrangement of linear irregular vessels and hairpin vessels surrounded by a whitish halo.

Our results show that dermoscopy can be considered a reliable tool to distinguish between well- and poorly differentiated cSCC. This distinction is characterized by an increase in predominantly arborizing vessels and a corresponding decrease in white structures as the tumor progresses from a well-differentiated to a poorly differentiated state. Moreover, the nodulo-ulcerative form demonstrates a central distribution of keratin, while the nodular form displays a diffuse distribution. Dermoscopy not only aids in accurate diagnosis but also provides valuable guidance to the anatomo-pathologist. Additionally, the implementation of dermoscopy offers economic benefits by streamlining the diagnostic process and facilitating timely and appropriate patient management, ultimately leading to improved prognosis.

Further studies are desirable to investigate the association between the different dermoscopic criteria and clinical form and even with the histological subtype of cSCC.

References

1. Bonerandi JJ, Monestier S. Carcinome épidermoïde (spinocellulaire) et ses précurseurs. *EMC – Dermatologie*. 2011;6:1–18. DOI : 10.1016/S0246-0319(11)56345-9.
2. Motaparthi K, Kapil JP, Velazquez EF. Cutaneous Squamous Cell Carcinoma: Review of the Eighth Edition of the American Joint Committee on Cancer Staging Guidelines, Prognostic Factors, and Histopathologic Variants. *Adv Anat Pathol*. 2017;24(4):171-194. DOI: 10.1097/PAP.0000000000000157. PMID: 28590951.
3. Fania L, Didona D, Di Pietro FR, et al. Cutaneous Squamous Cell Carcinoma: From Pathophysiology to Novel Therapeutic Approaches. *Biomedicines*. 2021;9:171. DOI: 10.3390/biomedicines9020171. PMID: 33572373. PMCID: PMC7916193.
4. Parekh V, Seykora JT. Cutaneous Squamous Cell Carcinoma. *Clin Lab Med*. 2017;37(3):503-525. DOI: 10.1016/j.cll.2017.06.003. PMID: 28802498.
5. Warszawik-Hendzel O, Olszewska M, Maj M, Rakowska A, Czuwara J, Rudnicka L. Non-invasive diagnostic techniques in the diagnosis of squamous cell carcinoma. *J Dermatol Case Rep*. 2015;9(4):89-97. DOI: 10.3315/jdcr.2015.1221. PMID: 26848316. PMCID: PMC4733351.
6. Yélamos O, Braun RP, Liopyris K, et al. Dermoscopy and dermatopathology correlates of cutaneous neoplasms. *J Am Acad Dermatol*. 2019;80:341-363. DOI:10.1016/j.jaad.2018.07.073. PMID: 30321581.
7. Saleh HM, Mokhtar MM, Mostafa AE. Dermoscopic criteria of squamous cell carcinoma in relation to clinical variant and histopathologic differentiation grade. *J Egypt Womens Dermatol Soc*. 2020;17:83-90. DOI: 10.4103/JEWD.JEWD_5_20
8. Lallas A, Pyne J, Kyrgidis A, et al. The clinical and dermoscopic features of invasive cutaneous squamous cell carcinoma depend on the histopathological grade of differentiation. *Br J Dermatol* 2015; 172:1308–1315. DOI: 10.1111/bjd.13510. PMID: 25363081.
9. Zalaudek I, Giacomel J, Schmid K, et al. Dermatoscopy of facial actinic keratosis, intraepidermal carcinoma, and invasive squamous cell carcinoma: a progression model. *J Am Acad Dermatol*. 2012;66(4):589-597. DOI: 10.1016/j.jaad.2011.02.011. PMID: 21839538.
10. Marghoob AA, Cowell L, Kopf AW, Scope A. Observation of chrysalis structures with polarized dermoscopy. *Arch Dermatol*. 2009;145(5):618. DOI: 10.1001/archdermatol.2009.28. PMID: 19451524.
11. Lin MJ, Pan Y, Jalilian C, Kelly JW. Dermoscopic characteristics of nodular squamous cell carcinoma and keratoacanthoma. *Dermatol Pract Concept*. 2014;4(2):9-15. DOI: 10.5826/dpc.0402a02. PMID: 24855567. PMCID: PMC4029247.
12. Zalaudek I, Argenziano G. Dermoscopy of actinic keratosis, intraepidermal carcinoma and squamous cell carcinoma. *Curr Probl Dermatol*. 2015;46:70-76. DOI: 10.1159/000366539. PMID: 25561209.
13. Lallas A, Argenziano G, Zendri E, et al. Update on non-melanoma skin cancer and the value of dermoscopy in its diagnosis and treatment monitoring. *Expert Rev Anticancer Ther*. 2013;13(5):541-558. DOI: 10.1586/era.13.38. PMID: 23617346.
14. Pyne J, Sapkota D, Wong JC. Squamous cell carcinoma: variation in dermatoscopic vascular features between well and non-well differentiated tumors. *Dermatol Pract Concept*. 2012;2(4):204a05. DOI: 10.5826/dpc.0204a05. PMID: 23785619. PMCID: PMC3663373.