

ANNEE 2017

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TITRE DE LA THESE

**DERMOSCOPIC FEATURES OF SUBUNGUAL SQUAMOUS CELL CARCINOMA:
A STUDY OF 44 CASES**

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présentée

à l'UFR des Sciences de Santé de Dijon
Circonscription Médecine

et soutenue publiquement le 17.03.17

pour obtenir le grade de Docteur en Médecine

par TEYSSEIRE Sandra

Née le 29/01/1989

A Guilhaierand-Granges

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Année Universitaire 2016-2017
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SERMENT D'HIPPOCRATE

« Au moment d'être admis(e) à exercer la médecine, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité.

Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux.

Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions.

J'interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité.

Même sous la contrainte, je ne ferai pas usage de mes connaissances contre les lois de l'humanité.

J'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences.

Je ne tromperai jamais leur confiance et n'exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences.

Je donnerai mes soins à l'indigent et à quiconque me les demandera.

Je ne me laisserai pas influencer par la soif du gain ou la recherche de la gloire.

Admis(e) dans l'intimité des personnes, je tairai les secrets qui me seront confiés. Reçu(e) à l'intérieur des maisons, je respecterai les secrets des foyers et ma conduite ne servira pas à corrompre les mœurs.

Je ferai tout pour soulager les souffrances. Je ne prolongerai pas abusivement les agonies. Je ne provoquerai jamais la mort délibérément.

Je préserverai l'indépendance nécessaire à l'accomplissement de ma mission. Je n'entreprendrai rien qui dépasse mes compétences. Je les entretiendrai et les perfectionnerai pour assurer au mieux les services qui me seront demandés.

J'apporterai mon aide à mes confrères ainsi qu'à leurs familles dans l'adversité.

Que les hommes et mes confrères m'accordent leur estime si je suis fidèle à mes promesses ; que je sois déshonoré(e) et méprisé(e) si j'y manque. »

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Liste des sigles ou abréviations

SSCC: Subungual Squamous Cell Carcinoma

HPV: Human Papilloma Virus

MRI: Magnetic Resonance Imaging

Dermoscopic features of subungual squamous cell carcinoma: A study of 44 cases

Introduction

Subungual tumors are rare in general. Of all malignant tumors, subungual squamous cell carcinoma (SSCC) is the most frequent one. Subungual SCC diagnosis is a challenge for dermatologists because of its multiple clinical features (1). Therefore, this tumor is often misdiagnosed as a viral wart, onychomycosis, post-traumatic dystrophy, subungual exostosis chronic paronychia, fibrokeratoma, onychopapilloma, onychomatricoma, melanoma, or subungual keratoacanthoma (2). It can lead to a delay in diagnosis and invasive cancer. Subungual SCC rarely metastasize, but local recurrences are common. This might be explained by the difficulties of its surgical treatment and to the frequently HPV-induced pathogeny of the tumor. Tumors have a higher rate of recurrence after excision than squamous cell carcinoma in other sites. Typically, one digit is involved; however, some studies have reported on simultaneous involvement of multiple digits (3). Metastases are rare with less than 10 cases reported (2). Radiography of the finger should systematically be performed, and magnetic resonance imaging (MRI) can help in doubtful cases (1). There is no standardized treatment for SSCC. The therapy of choice depends on the extent of the tumor. Lesions without bone involvement can be conservatively excised. Wide local excision has been proven effective, bears a lower risk of relapse and preserve quality of life and the functional abilities of the patient (1,4). Mohs micrographic surgery of the nail apparatus is challenging because of its unique anatomical and histological characteristics. Amputation of the distal phalanx is usually the recommended treatment for patients with bone infiltration or in case of deep margin involvement at histopathological examination of the specimen excised during conservative surgical treatment.

To confirm SSCC's diagnosis, an histopathological examination is necessary. Like in squamous cell carcinoma of the skin, it shows an atypical epithelial neoformation forming cordons of cells of squamous origin with frequent keratin pearls (5). Biopsy is painful and often leaves definitive dystrophic scars due to the surgical injury to the nail matrix. Therefore, more precise preoperative diagnosis is needed in order to select patients who will undergo the biopsy procedure.

Dermoscopy is currently used by experienced clinicians as a second-level procedure for the evaluation of pigmented or unpigmented skin lesions. Under these circumstances, dermoscopy has been shown to decrease the number of unnecessary excisions of benign lesions (6).

Dermoscopy is becoming more and more frequently utilized for the diagnosis of nail disorders (7–9). The unique anatomy of the nail apparatus makes nail dermoscopy technically difficult to be performed and not easy to be interpreted. Technical difficulties are due to the size, shape and hardness of the nail plate. Using this technique, one would be able to reduce the number of unnecessary surgeries and to choose the most adequate biopsy technique (10). However, little is known about dermoscopy of amelanotic nail tumors. Recently, dermoscopy shows its value in an unpigmented nail unit lesion: onychomatricoma (11). For these reasons, we decided to undertake this study of dermoscopic criteria of subungual squamous cell carcinoma based on 44 cases, assessing a set of 14 dermoscopic criteria.

The aim of this study was to define preoperative clinical and dermoscopic diagnostic criteria using non-invasive investigations in order to select patients for biopsy procedure. The second objective was to compare our results with those of a previous study about one of its principal differential diagnoses: onychomatricoma.

Materials and Methods

Patients

An unselected consecutive series of 44 cases of subungual squamous cell carcinoma in patients recruited in our center from 2007 to 2015 has been studied. All cases were retrieved from our clinical onychology database. Clinical images were taken with Canon EOS 350D camera with Canon 60mm EF-S macro lens and deported macro flash light (Canon France Paris). Dermoscopy images of the nail plate, the perionychium and, in most cases, of the free edge were taken with a Nikon Coolpix 995 (Champigny-sur-Marne, France) with a Derm-Lite FOTO lens (3Gen, San Juan Capistrano, Calif., USA). We systematically used a colourless jellified antiseptic solution (Purell gel; GOJO, Lille, France) for immersion. All pictures were taken with immersion + polarization photodermoscopy technique. Pathological results were retrieved. The following data were obtained from patients' records: age, sex, localization of the tumor and degree of invasion: in situ, microinvasive if tumor lobules were confined to the papillary dermis, or invasive.

Observers

A study group of 6 observers was constituted; all were trained in dermoscopy for several years. A preliminary study allowed us to determine 33 possibly relevant criteria on the basis of clinical and dermoscopic examination. Dermoscopy included the examination of the nail plate and perionychium, as well as the free edge of the nail plate. The 6 observers scored each criterion as present or absent without knowledge of the opinion of the others.

Criteria

All criteria with a representative picture are shown on **figures 1** and **2**.

The clinical criteria were as follows (**fig 1**): leuconychia, xanthonychia, erythronychia, paronychia, melanonychia, localized hyperkeratosis, thickening of the plate, longitudinal plate fracture, distal triangular fracture of the plate, overcurvature of the nail plate, localized crest transversal nail plate deformity, localized groove transversal nail plate deformity, localized crest longitudinal nail plate deformity, localized groove longitudinal nail plate deformity, splinter hemorrhages, proximal onycholysis, distal onycholysis, proximo-distal onycholysis, and tumoral lesion.

The dermoscopic criteria included the following (**fig 2**):

-for the nail plate examination: longitudinal parallel white lines, longitudinal parallel grey lines, sharply demarcated lesion edges, polycyclic/fuzzy lesion edges, parallel lesion edges, non-parallel lesion edges, hairpin-like vessels, splinter hemorrhages, rainbow sign and pink coloration of the background.

-for the dermoscopic examination of the plate free edge: dark dots, localized hyperkeratosis, free edge nail pitting and nail thickening.

Few unavailable data corresponded to missing information. Most of them concerned the free edge clinical and dermoscopic examination; in a few others, the lesser quality of the images did not permit to disclose the criterion. A criterion was considered as present if pointed out at least by 2 observers. Then, we compared our results with those of a previous study about 33 cases of onychomatricoma where 12 clinical and 12 dermoscopic criteria were evaluated. These 24 criteria were part of our 33 criteria.

Ethical committee approval:

This strictly observational retrospective study without expected or potential individual benefit for patients and investigators was not under the scope of the French Law (Huriet-Serusiclat / n° 88-1138 / 20th december 1988) and therefore required neither ethical committee approval nor inscription on an international clinical trial list.

This study has not been registered in public trial registry because it does not “prospectively assign human subjects to intervention or comparison groups to evaluate the cause and effect relationship between a medical intervention and a health outcome”.

Statistical analysis

Statistical analysis was conducted using the IBM SPSS 19.1 (IBM, Bois-Colombe, France). Logistic regression models were performed in terms of odds ratio (OR) and 95% confidence interval (CI).

Results

The characteristics of the patients are summarized in **table 1**. There were 22 males (50%) and 22 females (50%; male/female ratio=1). The age of the patients ranged from 32 to 88 years (mean 61.77). Overall, 25 (56.8%) arose on fingernails and 19 (43.2%) on the toenails. Histopathological examination showed in situ carcinoma in only 6 (13,6%) cases; 7 (15,9%) cases were micro-invasive and 31 (70,5%) were invasive. The precise localizations of the tumors are shown in **figure 3**. No case of multi-digital involvement was observed.

The clinical features of SSCC were variable. The most frequent were: distal onycholysis (68,2%) and localized hyperkeratosis (65,9%) (**fig 4**). About dermoscopic features, those most represented were: localized hyperkeratosis (90,9%), polycyclic/fuzzy lesion edges (79%), non-parallel lesion edges (65,1%), splinter hemorrhages (55,8%), longitudinal parallel white lines (55,8%) and nail thickening (54,5%) (**fig 5**). Evaluation of the other criteria reached a percentage of cases lower than 50.

Then, we compared those data to a previously published study (11), about preoperative diagnosis of onychomatricoma, using 24 of our 33 criteria (9 were not searched for in the previous study). We used logistic regression analyses to calculate the odds ratio (OR) and its corresponding 95% confidence interval (CI) for each criterion in SSCC and in onychomatricoma. Summarized results are presented in **table 2**.

Only one criterion was significantly associated with SSCC compared to onychomatricoma. It was about the plate free edge examination in dermoscopy: localized hyperkeratosis (OR=6,25, $p=0.012$, 95% CI [1,50-26,01]).

Statistically significant associations with onychomatricoma vs SSCC for clinical criteria were: thickening of the plate: OR=0,1, $p<0,001$, IC [0,03-0,31], overcurvature of the nail plate: OR=0,09, $p<0,001$, IC [0,03-0,3] and splinter hemorrhages: OR=0,1, $p<0,001$, IC [0,03-0,29]. Following dermoscopic criteria: longitudinal parallel white lines OR=0,28, $p=0,02$, IC [0,96-0,82], sharply demarcated lesion edges OR=0,24, $p=0,004$, IC [0,09-0,63], parallel lesion edges OR=0,03, $p<0,001$, IC [0,003-0,20], hairpin-like vessels OR=0,06, $p<0,001$, IC [0,12-0,28], splinter hemorrhages OR=0,28, $p=0,02$, IC [0,10-0,82], dark dots OR=0,22, $p=0,014$, IC [0,07-0,74] and free edge nail pitting OR=0,02, $p<0,001$, IC [0,003-0,10] were significantly higher among subjects with onychomatricoma.

Discussion

The diagnosis of unpigmented and pigmented tumors in the nail unit is difficult, and preoperative evaluation is crucial to precisely determine whether a lesion must be submitted to surgery or not and to establish the degree of emergency of the surgical management of the patient. The lack of awareness among physicians, its indolent natural history, and the higher prevalence of other benign conditions that simulate SSCC on the nail apparatus are responsible for delay in its diagnosis. The average delay for seeking medical advice was 6 years and 4 months (range 15 days– 39 years) in a 54 SSCC series of Lecerf *et al* (2).

For diagnosis of skin cancer, dermoscopy has been shown to be more accurate than naked-eye examination (6–12). In order to reduce the number of unnecessary surgeries and to choose the most adequate biopsy technique, nail dermoscopy was already validated for subungual melanoma (7–10,12). However, little is known about dermoscopy of amelanotic nail tumors (10).

This study was conducted to evaluate, aside from classically acknowledged clinical naked eye diagnostic criteria, dermoscopic features of SSCC through a series of observations in a large nail disease referral center.

As in previous reports, SSCC is found most commonly after the fifth decade (1,2,13). In the literature, it is twofold more frequently in men than in women (1,2,13). However, that was not found in our study with a sex ratio of 1. Most of cases were invasive. Subungual SCC mostly arises on the fingers and less commonly on the toes. According to Dalle *et al*, the most affected finger is the thumbnail and the majority of feet's cases occurred on the big toenail (1). Nevertheless, 2 similarly sized studies identified the right index and third fingers as the most commonly affected (2,13). For these authors, involvement of the first three fingers suggested a genital-digital HPV spread. Furthermore, Riddel *et al* (14) who reviewed HPV associated SSCC and periungual squamous cell carcinoma identified 28 patients (27,4%) with a history of HPV associated genital pathology or a similar history in a sexual partner. Physicians treating SSCC should be aware that their patients may be affected by another HPV induced-cancer. HPV vaccination campaigns may have an impact on the incidence of SSCC in the future. Multiple other predisposing factors, chronic paronychia, irradiation, sun exposure, trauma, arsenic exposure and congenital ectodermal dysplasia have been identified in the literature.

We observed varied clinical previously described (1,2) criteria in our 44 cases of SSCC. Two clinical naked eye examination criteria were frequently found: distal onycholysis and localized hyperkeratosis.

In contrast, more dermoscopic features were clearly frequently observed in our series of SSCC: localized hyperkeratosis, polycyclic/fuzzy lesion edges, non-parallel lesion edges, splinter hemorrhages, longitudinal parallel white lines and nail thickening. However some of these criteria cannot be considered as specific since they are also observed in others nail disease especially onychomatricoma. Our recently published series on dermoscopy of onychomatricoma (11) allowed us to underline that localized hyperkeratosis underneath the nail plate at free edge examination is statistically significantly associated with SSCC. On the opposite, parallel edges, sharp demarcation of the lesion and, to a lesser extent, presence of splinter hemorrhages at nail plate dermoscopic examination as well as free edge nail pitting at free edge dermoscopic examination can statistically significantly be considered as in favor of onychomatricoma. By contrast, we believe that the presence of unparallel lateral edges of the nail lesion or of fuzzy edges are more in favor of SSCC yet these criteria, not evaluated in our onychomatricoma study have not been statistically compared with our series of SSCC.

Another important differential diagnosis of SSCC is onychopapilloma. Only one published report by A. Tosti *et al.* focusses on clinical and dermoscopic features of this benign nail unit neoplasm (15). In their series of 47 cases of onychopapilloma, authors reported that dermoscopy of the distal edge disclosed a keratotic subungual mass in all cases. Curiously authors, in a table, opposed this finding to SSCC in which this feature is not observed yet their series was not comparative. Our data shows exactly the opposite since subungual keratotic material is found in 90% of our cases. In our view this is not surprising since we can hypothesize that this feature is due to the presence of a keratinizing tumor in the nail matrix that produces this material then driven underneath the nail plate towards the free edge. By contrast it could be hypothesized that SSCC devoid of this feature could be nail-bed derived and of not nail matrix origin. Nevertheless, on the basis of this report and published literature, differential diagnosis of onychopapilloma and SSCC remains difficult with many common criteria. Only fuzzy and unparallel borders, present in our series and not described in Tosti *et al.* publication could be candidates for being discriminant yet further studies are needed to clarify this point.

Others non-invasive diagnosis tools such as sonography and magnetic resonance (MR) have been studied (5). At ultrasonography, SSCC manifests as an heterogeneously hypoechoic focal mass with irregular margins. Erosions of the bone may be seen as well as tumor infiltration of adjacent tissue. Color Doppler ultrasonography can show low-resistance pulsatile flow signals within the tumor or at the tumor periphery. But, tissue characterization is limited, and detection can be hindered by artifacts, small tumor size, and flattened tumor shape. At MR imaging, SSCC demonstrates homogeneous hypointensity on T1-weighted images, intermediate signal intensity on T2-weighted images, and heterogeneous enhancement after gadolinium infusion. However, increased intramedullary signal intensity in the underlying bone is difficult to interpret (tumor invasion or reactive change?).

Conclusion:

We report herein the first large series of both clinically and dermoscopically-studied of subungual SCC. Our data suggest that dermoscopy of the nail plate and of the nail free edge provides usefull information: irregular and unparalleled borders, hyperkeratosis underneath the nail plate, splinter hemorrhages and white longitudinal lines, in order to better select patients to be submitted to biopsy. Since several of these criteria could be shared with onychopapilloma and onychomatricoma further comparative studies should be undertaken.

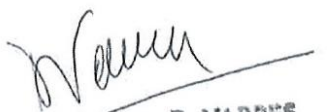
UNIVERSITE DE BOURGOGNE

THESE SOUTENUE PAR Mme TEYSSEIRE Sandra

CONCLUSIONS

Nous rapportons la première grande série ayant étudié les critères cliniques et dermoscopiques des carcinomes épidermoïdes de l'appareil unguéal et les ayant comparés à ceux de l'onychomatricome, qui constitue le principal diagnostic différentiel. Nos données suggèrent que la dermoscopie de la tablette unguéale et du bord libre de l'ongle est utile pour sélectionner les patients chez lesquels une biopsie unguéale doit être pratiquée pour rechercher un carcinome : bords irréguliers et non parallèles de la lésion, hyperkératose sous unguéale, hémorragies en flammèche et présence d'une bande blanche longitudinale. Des travaux ultérieurs permettraient de préciser ce travail en comparant les signes du carcinome épidermoïde unguéal avec ceux d'autres tumeurs kératinisantes telles que l'onychopapillome.

Le Président du jury,



Professeur P. VABRES
C.H.U. de DIJON
DERMATO-VENEREOLOGIE

Vu et permis d'imprimer

Dijon, le 21 Février 2017
Le Doyen, Pr. F.HUET



References:

1. Dalle S, Depape L, Phan A, Balme B, Ronger-Savle S, Thomas L. Squamous cell carcinoma of the nail apparatus: clinicopathological study of 35 cases. *Br J Dermatol*. 2007;156(5):871–874.
2. Lecerf P, Richert B, Theunis A, André J. A retrospective study of squamous cell carcinoma of the nail unit diagnosed in a Belgian general hospital over a 15-year period. *J Am Acad Dermatol*. 2013;69(2):253–261.
3. Porembski MA, Rayan GM. Subungual carcinomas in multiple digits. *J Hand Surg Eur Vol*. 2007;32(5):547–549.
4. Topin-Ruiz S. In press. *JAMA Dermatol*. 2017.
5. Baek HJ, Lee SJ, Cho KH, Choo HJ, Lee SM, Lee YH, et al. Subungual Tumors: Clinicopathologic Correlation with US and MR Imaging Findings. *RadioGraphics*. oct 2010;30(6):1621–36.
6. Argenziano G, Puig S, Zalaudek I, Sera F, Corona R, Alsina M, et al. Dermoscopy improves accuracy of primary care physicians to triage lesions suggestive of skin cancer. *J Clin Oncol*. 2006;24(12):1877–1882.
7. Ronger S, Touzet S, Ligeron C, Balme B, Viallard AM, Barrut D, et al. Dermoscopic examination of nail pigmentation. *Arch Dermatol*. 2002;138(10):1327–1333.
8. Thomas L, Dalle S. Dermoscopy provides useful information for the management of melanonychia striata. *Dermatol Ther*. 2007;20(1):3–10.
9. Hirata SH, Yamada S, Almeida FA, Enokihara MY, Rosa IP, Enokihara MMS, et al. Dermoscopic examination of the nail bed and matrix. *Int J Dermatol*. 2006;45(1):28–30.
10. Braun RP, Baran R, Le Gal FA, Dalle S, Ronger S, Pandolfi R, et al. Diagnosis and management of nail pigmentations. *J Am Acad Dermatol*. 2007;56(5):835–847.
11. Lesort C, Debarbieux S, Duru G, Dalle S, Poulhalon N, Thomas L. Dermoscopic features of onychomatricoma: a study of 34 cases. *Dermatology*. 2015;231(2):177–183.
12. Phan A, Dalle S, Touzet S, Ronger-Savle S, Balme B, Thomas L. Dermoscopic features of acral lentiginous melanoma in a large series of 110 cases in a white population. *Br J Dermatol*. 2010;162(4):765–771.
13. Tang N, Maloney ME, Clark AH, Jellinek NJ. A Retrospective Study of Nail Squamous Cell Carcinoma at 2 Institutions. *Dermatol Surg*. 2016;42:S8–S17.
14. Riddel C, Rashid R, Thomas V. Ungual and periungual human papillomavirus–associated squamous cell carcinoma: A review. *J Am Acad Dermatol*. 2011;64(6):1147–1153.
15. Tosti A, Schneider SL, Ramirez-Quizon MN, Zaiac M, Miteva M. Clinical, dermoscopic, and pathologic features of onychopapilloma: A review of 47 cases. *J Am Acad Dermatol*. mars 2016;74(3):521–6.

Table 1: Demographic characteristics of the patients and pathological data (n=44)

Gender		
Male		22 (50%)
Female		22 (50%)
Ratio (Male/Female)		1
Age, years		
Range		32-88
Mean		61.77
Median		63.5
Localization		
Hand		25 (56.8%)
Foot		19 (43.2%)
Ratio (Hand/Foot)		1.31
Degree of invasion		
In situ		6 (13,6%)
Micro-invasive		7 (15,9%)
Invasive		31 (70,5%)

Table 2: Comparison with a previously onychomatricoma study

Clinical criteria	SSCC	Onychomatricoma	OR	p-value	95%CI
	n/N(%)	n/N(%)			
leuconychia	19/44 (43,2)	20/33 (60,6)	0,49	0,132	NA
xanthonychia	14/44 (31,8)	12/32 (37,5)	0,78	0,607	NA
erythronychia	17/44 (38,6)	8/33 (24,2)	1,97	0,185	NA
paronychia	6/44 (13,6)	9/33 (27,3)	0,42	0,141	NA
melanonychia	12/44 (27,3)	6/32 (18,8)	1,63	0,391	NA
localized hyperkeratosis	29/44 (65,9)	13/22 (59,1)	1,34	0,588	NA
thickening of the plate*	9/44 (20,5)	18/25 (72)	0,1	<0,001	0,03-0,31
longitudinal plate fracture	12/44 (27,3)	3/33 (9,1)	3,75	0,057	NA
distal triangular fracture of the plate	11/44 (25)	5/33 (15,2)	1,87	0,296	NA
overcurvature of the nail plate*	5/44 (11,4)	17/29 (58,6)	0,09	<0,001	0,03-0,30
localized crest longitudinal nail plate deformity	9/44 (20,5)	16/28 (57,1)	0,64	0,062	NA
splinter hemorrhages*	7/44 (15,9)	21/32 (65,6)	0,10	<0,001	0,03-0,29
Dermoscopic criteria					
<i>Nail plate examination</i>					
longitudinal parallel white lines*	24/43 (55,8)	27/33 (81,8)	0,28	0,02	0,96-0,82
longitudinal parallel grey lines	21/43 (48,8)	18/33 (54,5)	0,8	0,622	NA
sharply demarcated lesion edges*	14/43 (32,6)	22/33 (66,7)	0,24	0,004	0,09-0,63
parallel lesion edges*	19/43 (44,2)	32/33 (97,0)	0,03	<0,001	0,003-0,20
hairpin-like vessels*	2/43 (4,7)	15/33 (45,5)	0,06	<0,001	0,12-0,28
splinter hemorrhages*	24/43 (55,8)	27/33 (81,8)	0,28	0,02	0,10-0,82
rainbow sign	0/43 (0)	4/33 (12,1)	NA	0,999	NA
pink coloration of the background	19/43 (44,2)	8/32 (25)	2,38	0,09	NA
<i>Plate free edge examination</i>					
dark dots*	16/33 (48,5)	21/26 (80,8)	0,22	0,014	0,07-0,74
localized hyperkeratosis*	30/33 (90,9)	16/26 (61,5)	6,25	0,012	1,50-26,01
nail pitting*	6/33 (18,2)	24/26 (92,3)	0,02	<0,001	0,003-0,10
nail thickening	18/33 (54,5)	26/26 (100)	0,79	0,363	NA

n= number of patients where the criterion was present

N= number total of valid patients

NA= non applicable

*= criterion with p-value<0,05

Figure 1: Clinical criteria



Leuconychia



Xanthonychia



Erythronychia



Paronychia



Melanonychia



Localized hyperkeratosis



Thickening of the plate



Longitudinal nail fracture



Distal triangular fracture of the plate



Overcurvature of the nail plate



Localized crest transversal



Localized groove transversal



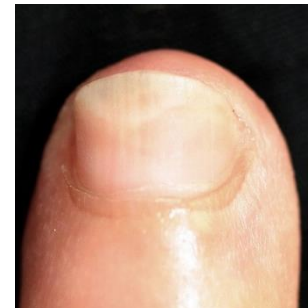
Localized crest longitudinal nail plate deformity



Localized groove longitudinal



Splinter hemorrhages



Distal onycholysis



Proximo-distal



Tumoral lesion

Figure 2: Dermoscopic criteria

-Nail plate examination



Longitudinal parallel white lines



Longitudinal parallel grey lines



Sharply demarcated lesion edges



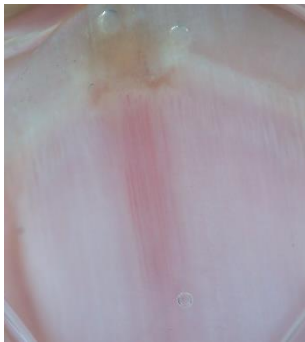
Polycyclic/fuzzy lesion edges



Parallel lesion edges



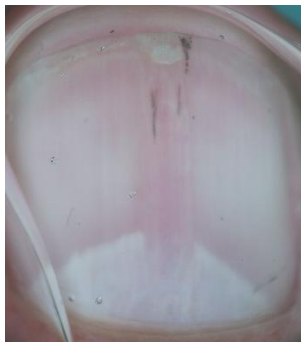
Non parallel lesion edges



Hairpin-like vessels

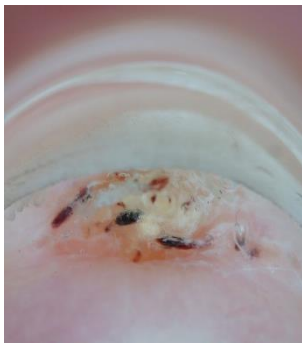


Splinter hemorrhages



Pink coloration of the background

-Plate free edge



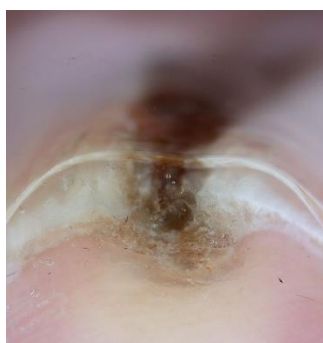
Dark dots



Localized hyperkeratosis



Free edge nail



Nail thickening

Figure 3: Precise localization of the tumors

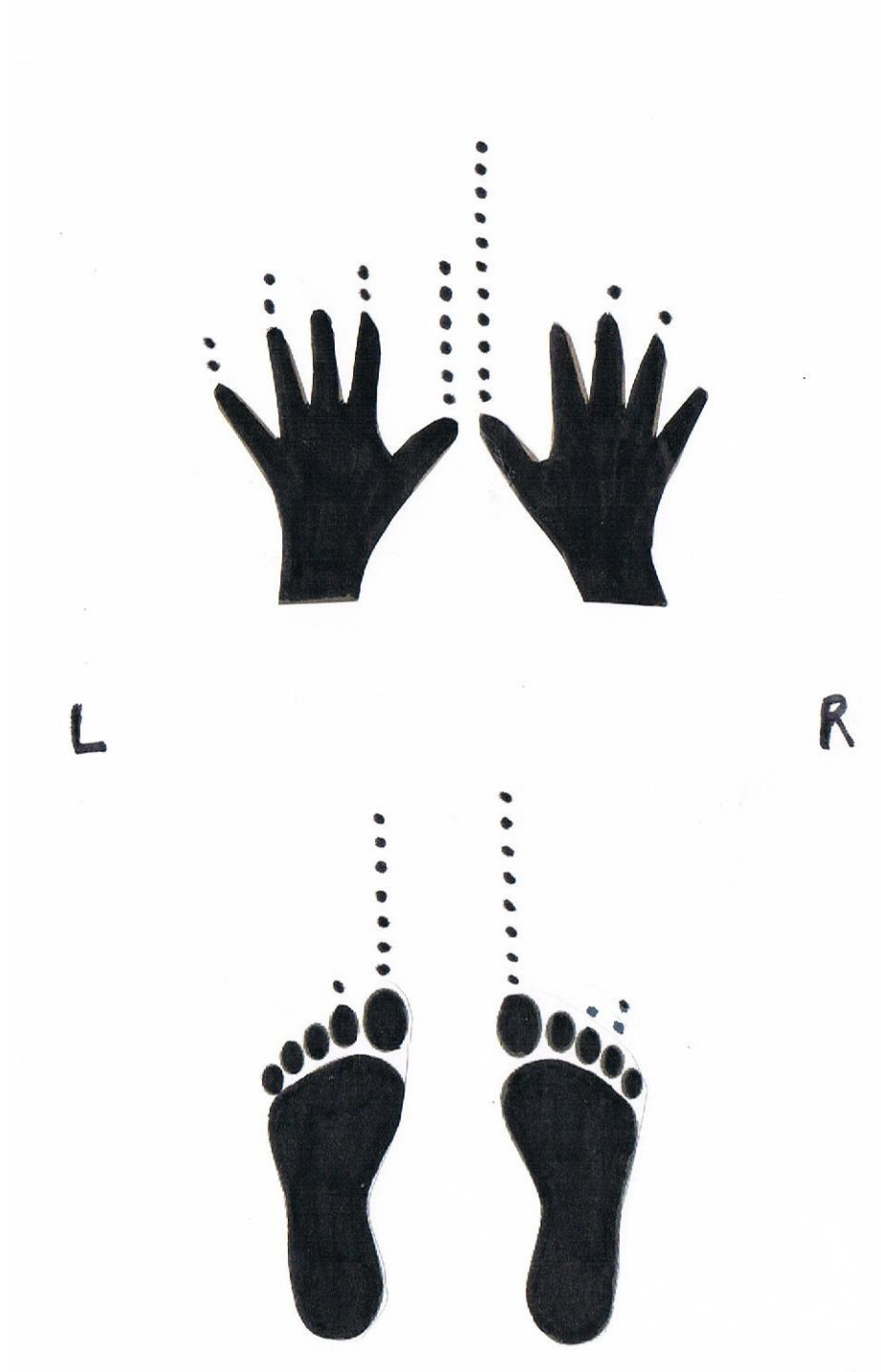


Figure 4: Clinical features of SSCC

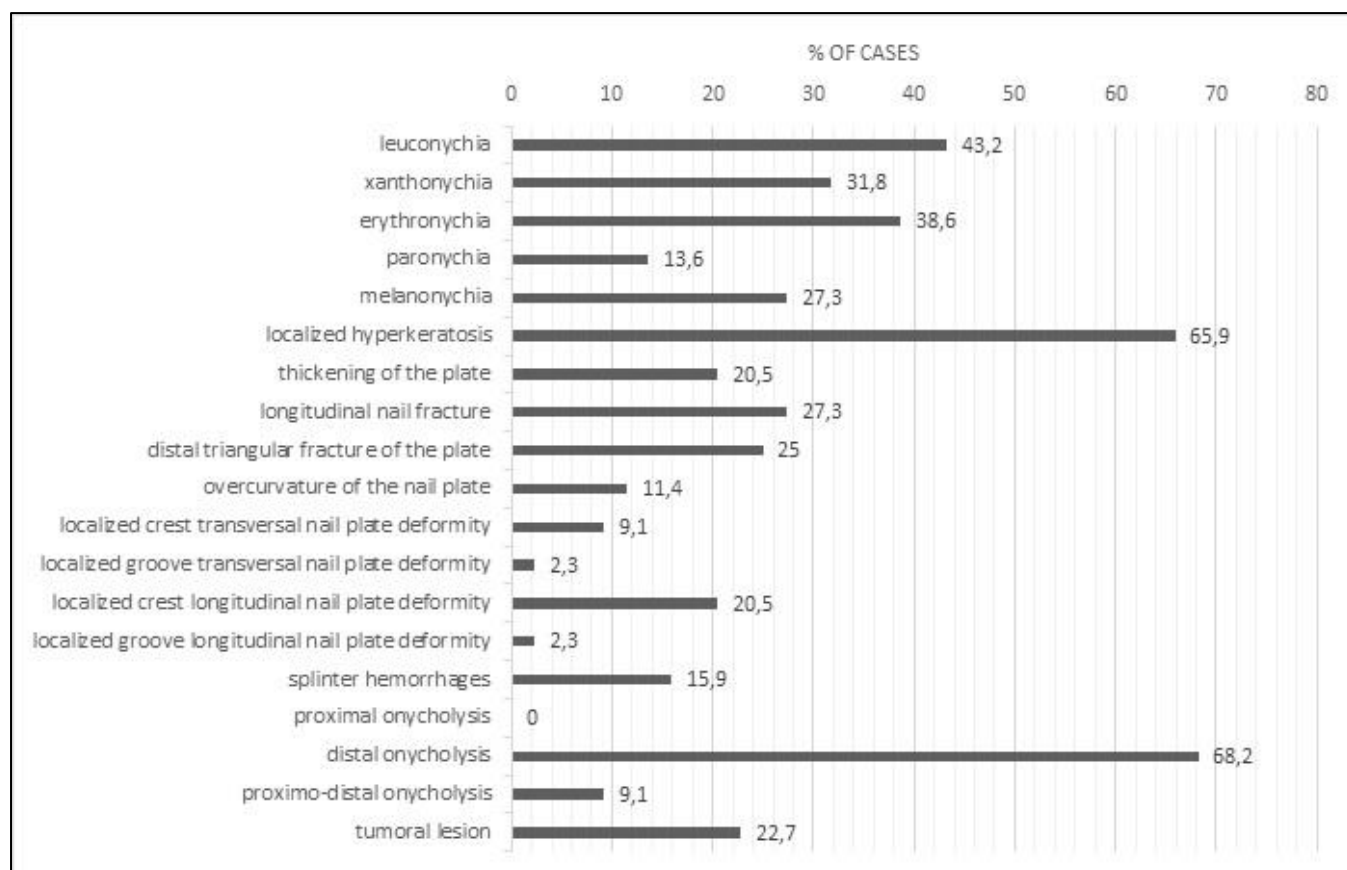
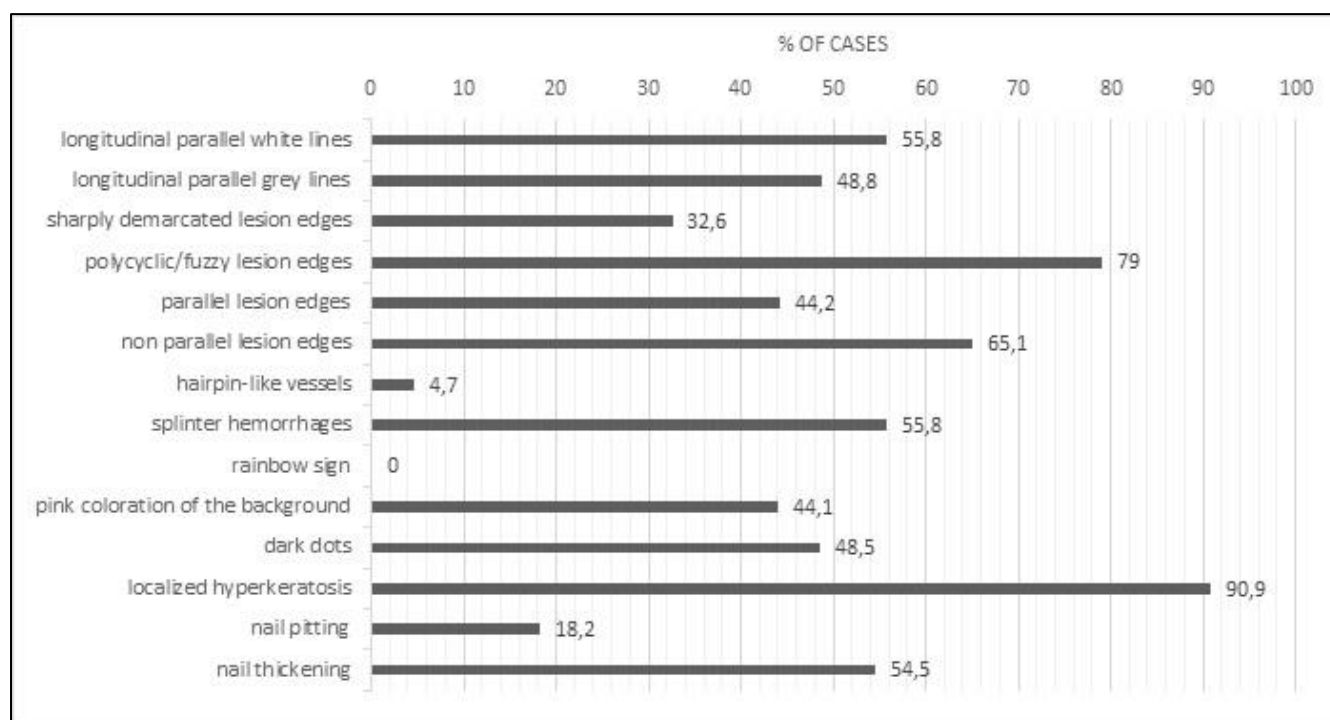


Figure 5: Dermoscopic features of SSCC



TITRE DE LA THESE: Les critères dermoscopiques du carcinome épidermoïde de l'appareil unguéal : une étude de 44 cas.

AUTEUR : TEYSSEIRE SANDRA

RESUME :

Introduction : Le carcinome épidermoïde est la plus fréquente des tumeurs malignes de l'appareil unguéal. Son diagnostic est difficile du fait de ses nombreuses présentations cliniques. Le diagnostic de certitude est porté grâce à une biopsie unguéale mais celle-ci est douloureuse et laisse souvent des cicatrices dystrophiques.

Objectifs : Définir les différentes présentations cliniques et dermoscopiques du carcinome épidermoïde unguéal et les comparer avec celles de l'onychomatricome.

Patients et Méthodes : Il s'agit d'une étude rétrospective de 44 cas de carcinomes épidermoïdes de l'appareil unguéal vus dans notre établissement sur une période de 8 ans. Pour chaque cas, 6 experts ont déterminé si 19 critères cliniques et 14 critères dermoscopiques prédéfinis étaient présents ou non. Nous avons ensuite comparé ces données avec celles publiées dans une étude précédente concernant l'onychomatricome.

Résultats : Seul un critère dermoscopique était significativement associé au diagnostic de carcinome épidermoïde unguéal en comparaison avec l'onychomatricome : l'hyperkératose localisée (OR=6,25, $p=0.012$, IC 95% [1,50-26,01]). A contrario, les bords parallèles de la lésion (OR=0,03, $p<0,001$, IC 95% [0,003-0,20]) et les bords nets de la lésion (OR=0,24, $p=0,004$, IC 95% [0,09-0,63]) étaient statistiquement en faveur de l'onychomatricome. Par déduction, nous supposons que la présence d'une lésion unguéale avec des bords non-parallèles ou flous est plutôt en faveur du diagnostic de carcinome épidermoïde de l'appareil unguéal.

Conclusion : La dermoscopie du carcinome épidermoïde de l'appareil unguéal est utile afin de mieux sélectionner les patients qui doivent bénéficier d'une biopsie.

MOTS-CLES : carcinome épidermoïde, dermoscopie, onychoscopie, tumeur maligne, ongle