Age, gender, and topography influence the clinical and dermoscopic appearance of lentigo maligna

Danica Tiodorovic-Zivkovic, MD,[a] Giuseppe Argenziano, MD,[c] Aimilios Lallas, MD,[c] Luc Thomas, MD,[d] Aleksandra Ignjatovic, MD,[b] Harold Rabinovitz, MD,[e] Elvira Moscarella, MD,[c] Caterina Longo, MD,[c] Rainer Hofmann-Wellenhof, MD,[f] and Iris Zalaudek, MD[f]

Nis, Serbia; Reggio Emilia, Italy; Lyon, France; Plantation, Florida; and Graz, Austria

Background: Little is known about the frequency of clinical and dermoscopic patterns of lentigo maligna (LM) in relation to specific anatomic subsites and patients characteristics.

Objective: We sought to assess the frequency of clinical and dermoscopic features of LM and to correlate them to specific anatomic subsites, and patients' age and gender.

Methods: This was a retrospective analysis of clinical and dermoscopic images of a series of consecutive, histopathologically diagnosed, facial and extrafacial LM.

Results: A total of 201 cases from 200 patients (mean age 69.51 ± 12.26 years) including 120 women were collected. Most cases were located on the face (n = 192, 95.5%). In 102 cases, LM presented as clinically solitary facial macule (s/LM), whereas it was associated with multiple surrounding freckles in the remaining cases. s/LM were significantly smaller (<10 vs >10 mm; P = .020) and associated with younger age compared with LM associated with multiple surrounding freckles (mean age 67.73 ± 12.68 years vs 71.34 ± 11.59 years, respectively; P = .036). Dermoscopically, gray color irrespective of a specific pattern was the most prevalent finding seen in 178 (88.6%) cases.

Limitations: This was a retrospective study.

Conclusions: The knowledge about patient age, patient gender, and site-related clinical features of LM associated with gray color upon dermoscopy may enhance the clinical recognition of LM.

Key words: dermoscopy; lentigo maligna.

The term "lentigo maligna" (LM) refers to melanoma in situ arising on chronically sun-damaged skin. The clinical diagnosis of early LM, even if coupled with dermoscopy, remains a challenge given its overlapping morphology with other pigmented macules that also commonly occur on sun-damaged skin. These include solar lentigo, flat seborrheic keratosis, freckles, lichen planus–like keratosis, and pigmented actinic keratosis.[1-8]

Up to date, little is known about the influence of age, gender, and topography on the clinical and dermoscopic variability of LM.[9]

In this study, we analyzed the morphological patterns including a recently introduced simple dermoscopic clue called "gray color"[10] in a series of consecutive, histopathologically proven facial and extrafacial LM and correlate these findings to patient demographics and lesion topography.

From the Clinic of Dermatovenereology, Clinical Center of Nis Medical Faculty,[a] and Department of Medical Statistics, Faculty of Medicine,[b] University of Nis; Skin Cancer Unit, Arcispedale S. Maria Nuova, IRCCS (Istituto Di Ricovero e Cura a Carattere Scientifico), Reggio Emilia[c]; Lyon 1 University, Dermatology Department, Centre Hospitalier Lyon Sud[d]; Skin and Cancer Associates, Plantation[e]; and Department of Dermatology and Venereology, Medical University of Graz.[f]

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Reprint requests: Iris Zalaudek, MD, Department of Dermatology and Venereology, Medical University of Graz, Auenbruggerplatz 8, 8036 Graz, Austria. E-mail: iris.zalaudek@gmail.com.

METHODS

We retrospectively collected consecutive cases of histopathologically proven facial and extrafacial LM diagnosed between January 2012 and January 2013 at 4 academic skin cancer clinics in France, Italy, Serbia, and the United States.

Requirements for study inclusion were the availability of high-resolution distant clinical overview photographs of the affected area, a clinical close-up photograph of the LM, and high-resolution digital dermoscopic images showing at least two thirds of the lesion surface. There were no limitations regarding the technical equipment used to take the clinical and dermoscopic images.

CAPSULE SUMMARY

- The clinical diagnosis of lentigo maligna is a challenge.
- The clinical and dermoscopic features of lentigo maligna are influenced by patient age and gender, and the lesion's specific anatomic subsite.
- Irrespective of specific dermoscopic patterns, gray color appears the single most important criterion in the diagnosis of lentigo maligna.

For each case, patients' demographics (ie, age, gender), specific anatomic location, and histopathological diagnosis were recorded. The face was subdivided into 4 main topographical areas, which were further subdivided into detailed anatomic subsites: (i) the upper aspect of the face subdivided into the front, temple, periocular region, and scalp; (ii) the nose subdivided into the cartilaginous and bone portion; (iii) the ears subclassified into the cartilaginous area, the periauricular region, and the earlobe; and (iv) the lower aspect of the face subdivided into the cheeks, perioral region, and chin. The local ethics committee at each center approved the study.

All clinical overview, close-up, and dermoscopic images were evaluated in consensus by 2 clinicians with more than 5 years of experience in skin cancer diagnosis and dermoscopy (D. T-Z. and A. L.) for predefined clinical and dermoscopic parameters. Both evaluators were aware of the study aim.

Analysis based on the clinical overview and close-up images included: (i) assessment of the clinical size (ie, <10 mm or >10 mm regarding the largest axis of the lesion) using a ruler as a reference measurement tool; (ii) assessment of whether LM presented as a solitary lesion (s/LM) on otherwise normal-appearing skin (ie, no additional pigmented macules are seen in the surrounding skin) or LM was associated with multiple surrounding pigmented freckles in the affected area; and (iii) laterality (ie, assessment whether the lesions were located on the left or right side of the face). Lesions located on the midline of the face or scalp and torso were not assigned to any of the sites.

All dermoscopic images were evaluated for the presence of predefined dermoscopic criteria, which are summarized in Table I and demonstrated in Fig 1.[10-12] If no consensus could be reached, the criterion was scored as absent.

Statistical analysis

Clinical and dermoscopic features were described with mean and SD or with frequency, as appropriate. Categorical variables were analyzed by χ^2 or Fisher exact tests and continuous data by the Student t test. Fisher exact test was used in cases where the expected values were less than 5 in the contingency table 2×2. Statistical analysis of data was performed using R 2.15.3 software (R Foundation for Statistical Computing, Vienna, Austria).[13]

RESULTS

Clinical findings

A total of 201 LM cases, seen in 200 patients (mean age 69.51 ± 12.26 years, range 28-99 years) were collected. There was a significant female predominance (n = 120; 60.0%; P = .008) among all patients. Table II shows the patients' demographics and clinical characteristics of LM.

Location on the cheek was significantly associated with female gender ($P < .001$), whereas a significant male predominance was found for location on the scalp (P = .025) and cartilaginous area on the ear (P = .025). No significant difference was seen between both genders regarding age, size, and laterality.

Of the 201 cases, 102 (50.7%) LM presented as a solitary lesion on normal-appearing skin (s/LM), whereas the remaining 99 (49.3%) cases were associated with surrounding freckles in the affected area (Fig 2). Patients with s/LM were significantly younger compared with LM associated with multiple surrounding freckles (mean age 67.73 ± 12.68 years, range 28-95 years, vs 71.34 ± 11.59 years, range 45-99 years, respectively; P = .036). s/LM cases were significantly smaller (ie, <10 mm) compared with LM cases associated with multiple surrounding freckles (P = .020); in detail, whereas 59.8% (n = 61) of s/LM

Table I. Dermoscopic criteria of lentigo maligna and their description

Dermoscopic criterion	Description
Gray color	Presence of gray color within the lesion
Asymmetric pigmented follicles	Gray circles within or around the follicular opening
Annular granular pattern	Gray dots and globules in between the follicular openings
Circle within a circle	Gray circle within the hair follicular surrounded by an outer gray to gray-brown circle
Pigmented rhomboidal structures	Brown to grayish lines or dots forming lines or rhomboids between the follicular openings
Darkening at dermoscopic examination	Observation on dermoscopic images of the presence of a color, invisible to the naked eye, and darker than all clinically observable shades of brown or gray
Targetlike pattern	Presence of a dark dot in the center of the hair follicle surrounded by a gray circle
Increased density of the vascular network	Vascular network of higher density within the lesion than in the peripheral skin
Red rhomboidal structures	Linear vessels occurring in the area separating the hair follicles from the others
Obliterated hair follicles	Structureless blue-gray areas within the follicular opening
White scarlike areas	White-gray structureless areas in between the follicular openings

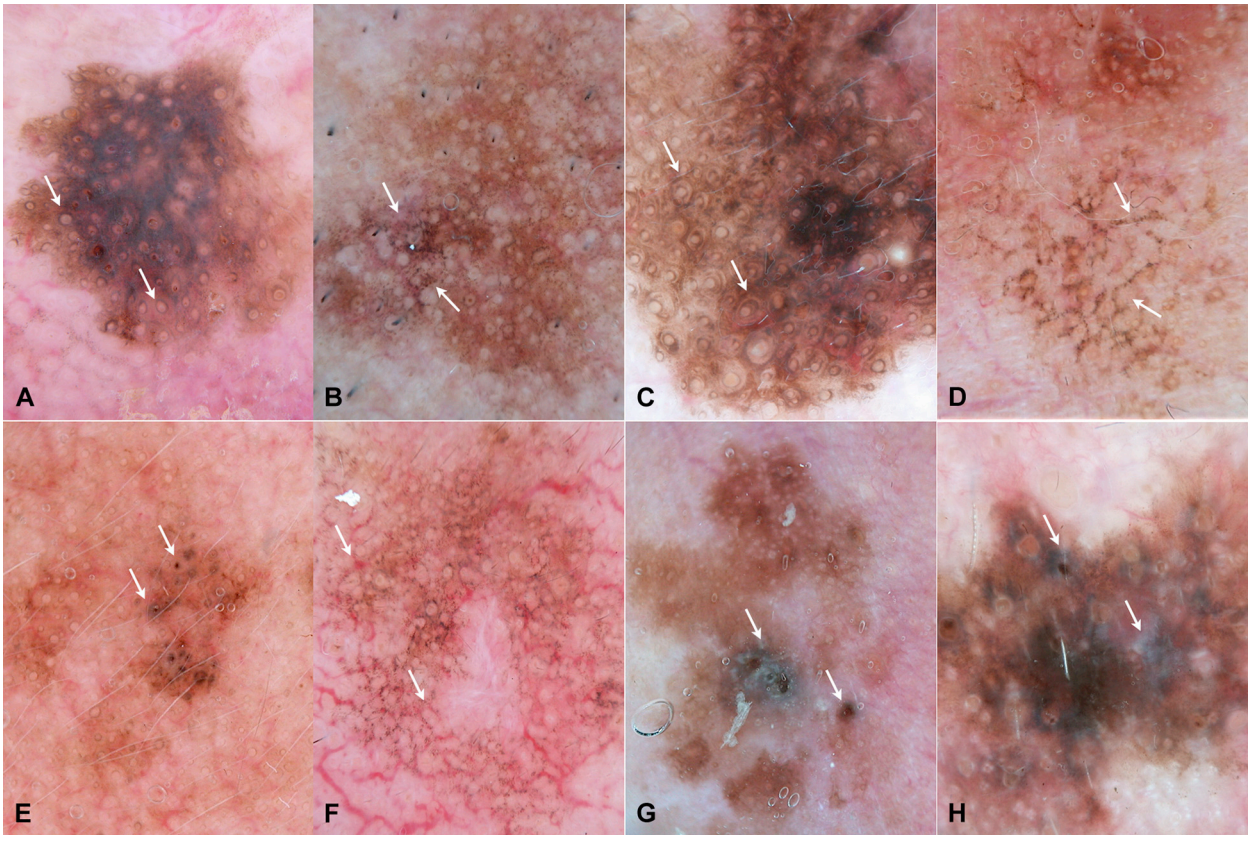

Fig 1. Examples showing the different dermoscopic criteria. **A**, Gray color and asymmetric pigmented follicular openings. **B**, Annular granular patterns. **C**, Circle within a circle. **D**, Pigmented rhomboidal structures. **E**, Targetlike patterns. **F**, Increased density of the vascular network and red rhomboidal structures. **G**, Obliterated hair follicles. **H**, White-gray scarlike areas.

Table II. Patient demographics, clinical features, and location of lentigo maligna by gender

	Total cases n = 201	M n = 81	F n = 120	*P* value (M vs F)
Demographic features				
Age, y	69.51 ± 12.26	69.98 ± 11.90	69.19 ± 12.54	.655
Clinical features				
Size				
<10 mm	103 (51.2%)	43 (53.1%)	60 (50.0%)	.775
>10 mm	98 (48.8%)	38 (46.9%)	60 (50.0%)	
Topography				
Upper aspect of face				
Front	21 (10.4%)	13 (16.0%)	8 (6.7%)	.058
Periocular	17 (8.5%)	3 (3.7%)	14 (11.7%)	.083
Scalp	4 (2.0%)	4 (4.9%)	0	.025*
Nose				
Cartilaginous	26 (13.0%)	15 (18.5%)	11 (9.2%)	.084
Bone	4 (2.0%)	2 (2.5%)	2 (1.7%)	.530
Ear				
Cartilaginous	4 (2.0%)	4 (4.9%)	0	.025*
Earlobe and preauricular	6 (3.0%)	5 (6.2%)	1 (0.8%)	.040*
Lower aspect of face				
Cheeks	108 (53.7%)	32 (39.5%)	76 (63.3%)	<.001
Perioral	2 (1.0%)	0	2 (1.7%)	.516*
Chin	0	0	0	-
Extrafacial				
Neck	9 (4.5%)	3 (3.7%)	6 (5.0%)	.742*
Arm	0	0	0	-
Solitary LM	102 (50.7%)	44 (43.1%)	58 (56.9%)	.491
LM in association with surrounding freckles	99 (49.3%)	37 (37.4%)	62 (62.6%)	

Frequencies are given as (%).
Age refers to mean ± SD.
F, Female; *LM*, lentigo maligna; *M*, male; *n*, absolute numbers.
*Fisher exact test.

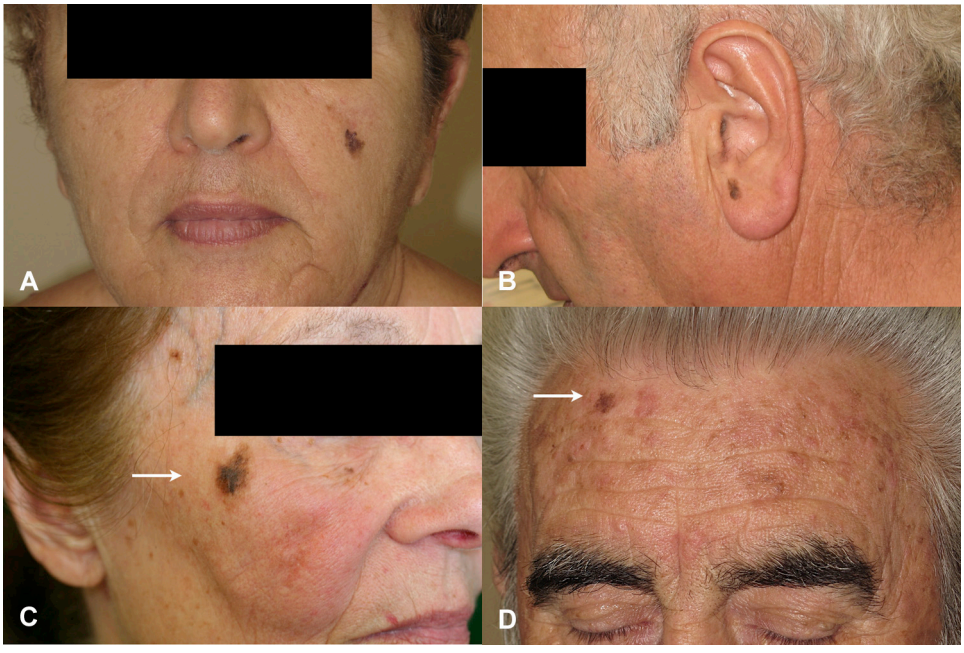

Fig 2. Lentigo maligna (LM) arising as solitary macule on the cheek (**A**) of a women and the earlobe (**B**) of a man. LM surrounded by other macules on the cheek (**C**) of a woman and the upper front aspect of the face (**D**) of a man.

measured less than 10 mm in size, 57.6% (n = 58) of LM associated with multiple surrounding freckles measured greater than 10 mm.

Dermoscopic findings

Table III summarizes the frequency of dermoscopic patterns in LM cases by gender and dermoscopic features of LM in relation to the specific anatomic subsites. The most frequent dermoscopic feature was gray color, which was seen in 178 (88.6%) cases overall, irrespective of the gender (Fig 3).

Significant gender-related differences in the frequency were found for circle within a circle (P = .009) and the targetlike pattern (P = .001).

Analysis regarding the morphological patterns and specific subsites revealed significant associations between asymmetrical pigmented hair follicles and the lower part of the face (P = .036) compared with other locations, for pigmented rhomboidal structures and the upper part of the face (P = .028) compared with the lower part of the face, and the targetlike structures and location on the ear (P = .010) and the nose (P = .026) compared with the upper part of the face (Table III).

DISCUSSION

Our study suggests that the morphological appearance of LM is influenced by patients' age and gender, and by the anatomic subsite.

In line with previous studies,[1,3,14,15] we found a significant female predominance among patients with LM, but the female predominance was significant only for LM arising on the cheeks. In contrast, location on the scalp and the nose were significantly associated with men. This observation is similar to the data reported by Lesage et al,[9] who found the great majority of melanomas in women occurring on the central areas of the face (including cheek as the most common site), whereas men more commonly developed tumors on a lateral location. A further detailed comparison of their and our results is limited by the inclusion of invasive LM melanomas, superficial spreading and nodular subtypes in their study, whereas we included only LM cases. Nevertheless, comparing our findings with only their in situ cases, which comprised 54.2% of their data set,[9] reveals some noteworthy differences (Table IV).

First, in their study, the front and temple appeared the second most frequent site of in situ melanomas; in contrast, we encountered the nose as the second most commonly affected site. Noteworthy LM occurred in the vast majority of our cases (86.7%) on the front cartilaginous portion of the nose and affected as much as twice as many men compared with women in our study.

Second, in their study melanomas located on the peripheral areas of the body showed a significant right and left side predominance in women and men, respectively. In contrast we found a balanced left-right distribution between both genders.

A novel observation in our study is that more than half of our LM cases developed as solitary lesion on clinically normal-appearing skin. These lesions were smaller and associated with younger age compared with LM arising in association with multiple surrounding freckles. This could be related to an earlier clinical detection of LM by means of dermoscopy compared with the unaided eye, as dermoscopy is used as standard diagnosis in all participating centers. In fact, a recent study investigating the diameter of clinically diagnosed LM referred for surgery reports on a mean diameter of 21 ± 10 mm.[16] However, this explanation implies also that LM may develop much earlier in life, before clinical signs of actinic damage such as solar lentigines or actinic keratosis become clinically manifest.

We also found some significant differences in the frequency of dermoscopic patterns and specific subsites. Variations in the specific skin anatomy may account for these differences but further studies are needed to correlate specific dermoscopic structures to the underlying histologic characteristics of the skin anatomy.

Nevertheless, in line with previous reports[10,17,18] our study reveals that the presence of gray color, irrespective of the associated dermoscopic pattern, may be regarded an important dermoscopic clue, albeit not highly specific, for the diagnosis of LM and should prompt clinicians to perform a biopsy.[10,17]

Our study has some limitations. First, the retrospective design does not allow any conclusions about patients' sun-exposure habits, which might have an influence on the topography. Second, the comparison of our findings and the data reported by Lesage et al[9] is limited by differences in the study design and methodology. Third, the high frequency of solitary lesions in our study may be related to our study cohort, which included about two thirds of residents of middle European countries. Accordingly, our results cannot be transferred to other populations. Fourth, we cannot exclude that the number of small lesions in daily practice may be even higher as reported herein as most of the included cases were collected from secondary or tertiary referral centers, in which surgically difficult manageable lesions may be overrepresented. Finally, no conclusions can be extracted from our study on the value of the clinical and dermoscopic criteria related to LM for its discrimination from other skin tumors on the face. However, a recent

Table III. Absolute numbers and frequencies (%) of dermoscopic criteria among lentigo maligna cases by gender and in relation to the specific anatomic subsites

Dermoscopic features	M n = 81	F n = 120	*P* value (M vs F)	Upper aspect of face n = 42	Nose n = 30	Ears n = 10	Lower aspect of face n = 110	Extrafacial n = 9	*P* value
Gray color	72 (88.9%)	106 (88.3%)	.903	40 (95.2%)	25 (83.3%)	10 (100.0%)	94 (85.5%)	9 (100.0%)	.071
Asymmetric pigmented follicular openings	40 (49.4%)	49 (40.8%)	.293	13 (31.0%)	15 (50.0%)	4 (40.0%)	56 (50.9%)	1 (11.1%)	.036
Annular granular pattern	17 (21.0%)	38 (31.7%)	.132	8 (19.0%)	7 (23.3%)	3 (30.0%)	36 (32.7%)	1 (11.1%)	.306
Circle within a circle	29 (35.8%)	22 (18.3%)	.009	11 (26.2%)	12 (40.0%)	3 (30.0%)	23 (20.9%)	2 (22.2%)	.348
Pigmented rhomboidal structures	16 (19.8%)	20 (16.7%)	.710	3 (7.1%)†	3 (10.0%)	3 (30.0%)	27 (24.5%)	0	.028
Darkening at dermoscopic examination	1 (1.2%)	2 (1.7%)	.644*	0	0	0	3 (2.7%)	0	.455
Targetlike pattern	25 (30.9%)	14 (11.7%)	.001	4 (9.5%)‡§	10 (33.3%)	5 (50.0%)	20 (18.2%)	0	.005
Increased density of the vascular network	11 (13.6%)	19 (15.8%)	.812	10 (23.8%)	3 (10.0%)	2 (20.0%)	12 (10.9%)	3 (33.3%)	.164
Red rhomboidal structures	0	4 (3.3%)	.150*	0	0	1 (10.0%)	3 (2.7%)	0	.265
Obliterated hair follicles	12 (14.8%)	13 (10.8%)	.535	3 (7.1%)	6 (20.0%)	2 (20.0%)	13 (11.8%)	1 (11.1%)	.537
White scarlike areas	12 (14.8%)	16 (13.3%)	.928	5 (11.9%)	3 (10.0%)	1 (10.0%)	19 (17.3%)	0	.357

Frequencies in columns refer to the percentage of cases in the respective category.
F, Female; *M*, male.
*Fisher exact test.
†Upper vs lower aspect of face $P = .028$.
‡Upper aspect of face vs ear $P = .010$.
§Upper aspect of face vs nose $P = .026$.

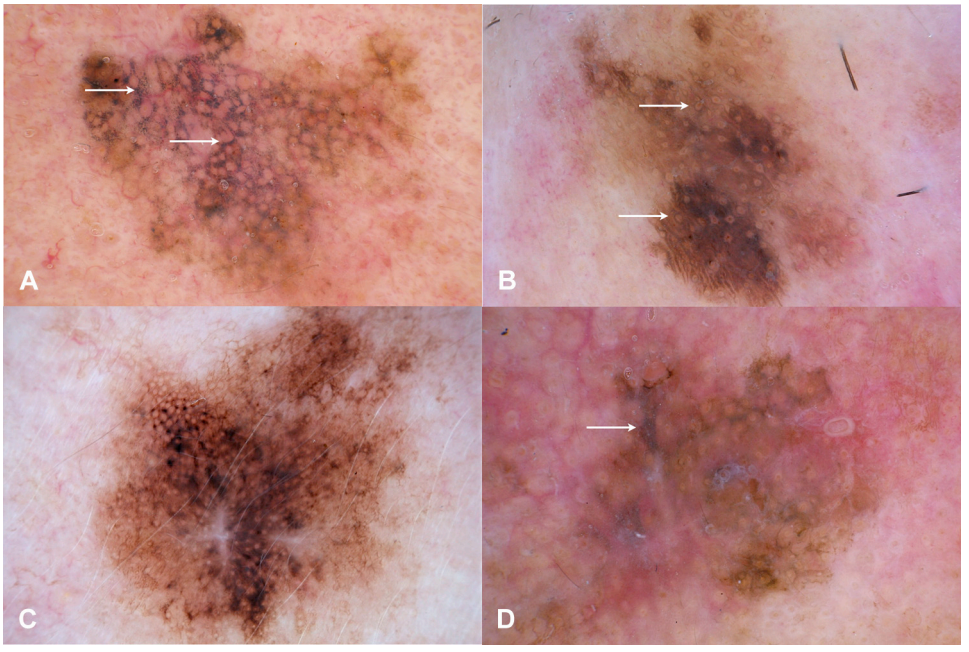

Fig 3. Dermoscopic features of lentigo maligna (LM) as shown in Fig 2. All cases are characterized by gray color. **A**, LM showing gray annular granular structures. **B**, LM showing gray asymmetrical pigmented follicles and circle within a circle. **C**, LM characterized by a brown to gray pseudonetwork pattern and black globules. **D**, LM characterized by gray rhomboidal lines around the hair follicles.

Table IV. Comparison of gender- and side-related differences in the topography of lentigo maligna in the study by Lesage et al[9] and the current study

Location	Men (current study) n = 81	Men (Lesage et al[9]) n = 50	Women (current study) n = 120	Women (Lesage et al[9]) n = 75	Total cases (current study) n = 201	Total cases (Lesage et al[9]) n = 125
Upper aspect of face						
Front/temple	13 (16.0%)	9 (18.0%)	8 (6.7%)	8 (10.7%)	21 (10.4)	17
Periocular	3 (3.7%)	5 (10.0%)	14 (11.1%)	2 (2.7%)	17 (8.5)	7
Scalp	4 (4.9%)	1 (2.0%)	0	0	4 (2.0)	1
Nose						
Cartilaginous	15 (18.5%)	6 (12.0%)	11 (9.2%)	2 (2.7%)	26 (13.0)	8
Bone	2 (2.5%)		2 (1.7%)		4 (2.0)	
Ear						
Cartilaginous	4 (4.9%)	6 (12.0%)	0	3 (4%)	4 (2.0)	9
Earlobe and preauricular	5 (6.2%)		1 (0.8%)		6 (3.0)	
Lower aspect of face						
Cheeks	31 (38.3%)	20 (40.0%)	77 (64.2%)	54 (72%)	108 (53.7)	74
Perioral	0	1 (2.0%)	2 (1.7%)	5 (6.7%)	2 (1.0)	6
Chin	0		0		0	
Extrafacial						
Neck	3 (3.7%)	2 (4.0%)	6 (5.0%)	1 (1.3%)	9 (4.5)	3
Arm	0	0	0	0	0	0
Left side	37 (45.7%)	34 (57.6%)	60 (50.0%)	7 (26.9%)	97 (48.2)*	
Right side	37 (45.7%)	25 (42.4%)	55 (45.8%)	19 (73.1%)	92 (45.8)	

*A total of 12 (6.0%) cases (7 men and 5 women) were not assigned laterality because of location at the midline.

study reported on asymmetrical pigmented hair follicles (gray circles) having the highest positive predictive value for LM (31.3%, 95% confidence interval 11.1-58.6).[18]

In summary, our study supports the following practical recommendations: (1) clinicians should not exclude the diagnosis of LM when observing a solitary macule on clinically nonphotodamaged,

normal-appearing skin or at relatively young age; (2) LM most commonly arises on the cheeks of women, whereas it prevails on the scalp and on the cartilaginous proportion of the ears in men; and (3) biopsy is recommended when dermoscopic examination discloses gray color.

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