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Original article

Clinical and Dermoscopic Features of Lentigo Maligna

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SUMMARY

Introduction/Aim. Lentigo maligna (LM) represents an *in situ* melanoma that develops on chronically photo-damaged skin. Clinical diagnosis of LM is often difficult, even for experienced dermatologists. The aim of the study was to analyze the clinical and dermoscopic features of patients with pathohistologically verified lentigo maligna (LM) and to determine a possible influence of anatomical topography, age and gender in the dermoscopic features of LM.

Patients and methods. This retrospective study included 32 patients with 32 LM changes in total, diagnosed between 2017 and 2020. Clinical data recorded from each patient included the following: demographic features (age, gender), anatomic localization (facial or extrafacial) and clinical size (< 10 mm or > 10 mm). Facial area was subdivided into eight topographical sites, while extrafacial localization involved any location outside the face region. All dermoscopic images were analyzed for the presence of dermoscopic features previously described as LM.

Results. In the total of 32 patients, there were 19 males and 13 females. The patients' age ranged from 34 to 80 years (median age 60.1 ± 10.4 years). Significant female predominance was observed for localization on the cheeks (p = 0.018). Localization on the nose was significantly associated with patients older than 65 (p = 0.039). The most frequent dermoscopic features were asymmetric pigmented follicular openings in 23 (71.9%) cases, gray color in 22 (68.8%) and pigmented rhomboidal structures in 15 (46.9%) cases. In relation to age and specific dermoscopic features, gray color (p = 0.035) and white scar-like areas (p = 0.012) were significantly higher in patients older than 65, while pigmented rhomboidal structures (p = 0.041) were significantly associated with younger patients.

Conclusion. The observed differences in the frequency of clinical and dermoscopic features of LM have significant importance in everyday clinical practice and can assist clinicians in the early diagnosis of this malignant tumor.

Keywords: **lentigo maligna, dermoscopy, differential**

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INTRODUCTION

Lentigo maligna (LM) is an *in situ* form of melanoma predominantly located on the face. The incidence of this neoplasm has been increasing in recent years due to the changes in sun exposure habits and increased life expectancy (1, 2). This form of melanoma was first described in 1892 by the British surgeon Jonathan Hutchinson as "senile spot". Soon, the term "Hutchinson's melanotic spot" was coined as a colloquial name for this malignant tumor, but later Hutchinson himself suggested "lentigo melanosis" as the most suitable term. The French dermatologist Dubreuilh proposed the name "melanose circumscrite precancereuse" in 1912, and finally, in 1948, Becker named this malignant pigmented lesion lentigo maligna (1 - 4).

Some authors have previously proposed dividing LM into a pre-malignant lesion (Hutchinson's melanotic spot) and an *in situ* (LM) stage of melanoma, implying a different risk for the development of invasive melanoma (5). Today, the term LM refers exclusively to the *in situ* phase of melanoma. If LM is not diagnosed at its earliest stage, it turns into an invasive form, known as lentigo maligna melanoma (LMM), which accounts for 4 - 15% of all cutaneous melanomas (5 - 7). Given that LMM has the same prognosis as other invasive melanomas, early detection of LM is essential for reducing the mortality of this malignant disease.

LM and LMM are both considered to occur as a result of chronic cumulative photo-exposure and typically appear on photo-exposed and photo-damaged skin of middle-aged and elderly people, although their incidence in younger population has increased in recent years. In addition to the typical localization on the photo-damaged skin of the head and neck, LM can be sometimes found on the trunk and extremities (5 - 9).

AIMS

The aim of our study was to analyze the clinical and dermoscopic features of patients with pathohistologically verified LM and to determine possible influence of anatomical topography, age and gender in the dermoscopic features of LM.

PATIENTS AND METHODS

This retrospective observational study included a total of 32 patients with previously histopathologically verified cases of LM, collected at the Clinic of Dermatovenereology, University Clinical Center Niš, between 2017 and 2020.

Clinical data recorded from each patient included the following: demographic features (age, gender), anatomic localization (facial or extrafacial) and clinical size (< 10 mm or > 10 mm according to the largest axis) (Figure 1). Regarding the lesion localization, facial area was subdivided into eight topographical sites, including: scalp, frontal area, ears, cheeks, nose, chin, perioral and periorbital area, while extrafacial localization involved any location outside the face region. Dermoscopy examination was performed using Nikon Coopix 4500 digital camera (Nickon Corporation, Japan) coupled with DermLite FOTO dermoscope at 10-fold magnification. All dermoscopic images were analyzed for the presence of dermoscopic features previously described as LM (Figure 1) (10 - 14).

Clinical and dermoscopic features were presented as mean, standard deviation, minimum and maximum values, or in the form of absolute and relative numbers. The differences between subcategories were evaluated with Chi-square test or Fisher's exact probability test. The hypothesis was tested with a significance threshold of $p < 0.05$. Statistical data analysis was performed in the IBM SPSS 20.0 software package.

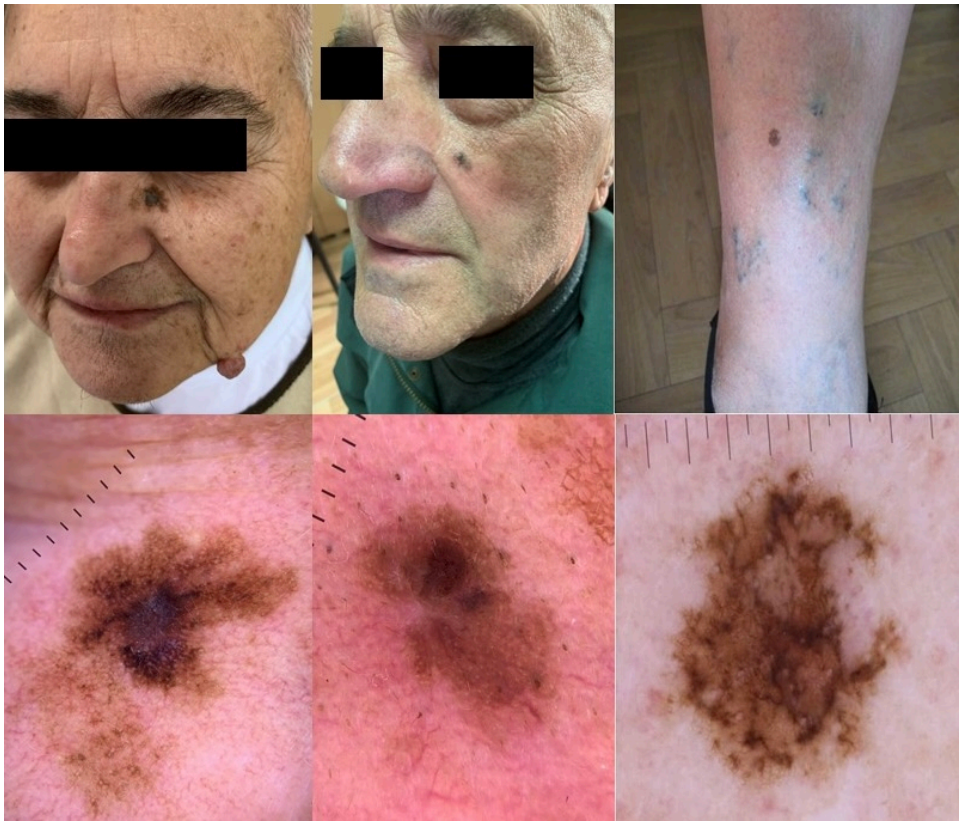

Figure 1. *Clinical and dermscopic features of facial LM and extrafacial LM*

RESULTS

A total of 32 pathohistologically confirmed LM lesions from 32 patients were analyzed, including 19 male (59.4%) and 13 female (40.6%) patients. The age of the patients ranged from 34 to 80 years (median age 60.1 ± 10.4 years). There was a higher predominance for LM on the facial area compared to the extrafacial localization [(28 (87.5%) vs. 4 (12.5%)]. Regarding the facial localization, the most commonly involved areas were cheeks in 13 (40.6%) cases, ears in 4 (12.5%) and nose in 4 (12.5%) cases. Significant female predominance was observed for the localization on the cheeks [9 (69.2%) vs. 4 (21.1%), (p = 0.018)]. In patients younger than 65, LM was most commonly found on the cheeks in 11 (45.8%) and ears in 3 (12.5%) cases, while nose and cheeks were a predominant localization for patients older than 65 in 3 (37.5%) and 2 (25.5%) cases, respectively. Localization on the nose was significantly associated with patients older than 65 (p = 0.039). No significant difference was observed in the clinical size of LM regarding the gender and age of the patients. Detailed clinical and demographic features are shown in Tables 1 and 2.

Dermoscopic features are summarized in Tables 3 and 4. The most frequent dermoscopic features were asymmetric pigmented follicular openings in 23 (71.9%), gray color in 22 (68.8%) and pigmented rhomboidal structures in 15 (46.9%) cases. No significant difference was noticed between specific dermoscopic features and gender. Namely, both gray color and asymmetric pigmented follicular openings [14 (73.7%) vs. 8 (61.5%); 11 (57.9% vs. 12 (92.3%)] were dominant in male and female patients, respectively. In relation to age and specific dermoscopic features, gray color [8 (100.0%) vs. 14 (58.3%), p = 0.035] and white scar-like areas were [5 (62.5.0%) vs. 3 (12.5%), p = 0.012] significantly higher in patients older than 65, while pigmented rhomboidal structures [14 (58.3%) vs. 1 (12.5%), p = 0.041] were significantly associated with younger patients.

Table 1. *Clinical features and topography of LM lesions*

	Total cases n = 32	M n = 19	F n = 13	P value[1] M vs F
Clinical features				
Size				
< 10 mm	14 (43.8%)	8 (42.1%)	6 (46.2%)	1.000
> 10 mm	18 (56.2%)	11 (57.9%)	7 (53.8%)	
Topography				
Scalp	3 (9.4%)	2 (10.5%)	1 (7.7%)	1.000
Frontal area	1 (3.1%)	0 (0.0%)	1 (7.7%)	0.406*
Ears	4 (12.5%)	3 (15.8%)	1 (7.7%)	0.629*
Cheeks	13 (40.6%)	4 (21.1%)	9 (69.2%)	0.018
Nose	4 (12.5%)	4 (21.1%)	0 (0.0%)	0.128*
Chin	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Periocular area	2 (6.2%)	2 (10.5%)	0 (0.0%)	0.502*
Periorbital area	1 (3.1%)	1 (5.3%)	0 (0.0%)	1.000*
Extrafacial location	4 (12.5%)	3 (15.8%)	1 (7.7%)	0.629

*Fisher exact test

[1]Chi-squared test

M, Male; LM, lentigo maligna; F, female. n, absolute number

Table 2. *Clinical features and topography of LM regarding the age of patients*

	Under 65 years n = 24	Above 65 years n = 8	P value[1]
Clinical features			
Size			
< 10 mm	12 (50.0%)	2 (25.0%)	0.411
> 10 mm	12 (50.0%)	6 (75.0%)	
Topography			
Scalp	1 (4.2%)	2 (25.0%)	0.147*
Frontal area	1 (4.2%)	0 (0.0%)	1.000*
Ears	3 (12.5%)	1 (12.5%)	1.000*
Cheeks	11 (45.8%)	2 (25.0%)	0.533
Nose	1 (4.2%)	3 (37.5%)	0.039
Chin	0 (0.0%)	0 (0.0%)	
Periocular area	2 (8.3%)	0 (0.0%)	1.000*
Periorbital area	1 (4.2%)	0 (0.0%)	1.000*
Extrafacial location	4 (16.7%)	0 (7.7%)	0.550*

*Fisher exact test

[1]Chi-squared test

M, Male; LM, lentigo maligna; F, female. n, absolute number

Table 3. *Dermoscopic features of LM*

	Total cases n = 32	M n = 19	F n = 13	P value[1] M vs F
Dermoscopic features				
Gray color	22 (68.8%)	14 (73.7%)	8(61.5%)	0.734
Asymmetric pigmented follicular openings	23 (71.9%)	11 (57.9%)	12(92.3%)	0.050*
Annular granular pattern	8 (25.0%)	4 (21.1%)	4 (30.8%)	0.835
Circle within a circle	2 (6.3%)	2 (10.5%)	0 (0.0%)	0.502*
Pigmented rhomboidal structures	15 (46.9%)	9 (47.4%)	6 (46.2%)	1.000*
Darkening at dermoscopic examination	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Target-like pattern	1 (3.1%)	1 (5.3%)	0 (0.0%)	1.000
Increased density of vascular network	6 (18.8%)	3 (15.8%)	3 (23.1%)	0.954
Red rhomboidal structures	2 (6.3%)	0 (0.0%)	2 (15.4%)	0.157*
Obliterated hair follicles	8 (25.0%)	4 (21.1%)	4 (30.8%)	0.835
White scar-like areas	8 (25.0%)	6 (31.6%)	2 (15.4%)	0.533
Globules/dots	7 (21.9%)	5 (26.3%)	2 (15.4%)	0.671*

*Fisher exact test

[1]Chi-squared test

M, Male; LM, lentigo maligna; F, female. n, absolute number

Table 4. *Dermoscopic features of LM regarding the age of patients*

	Under 65 years n = 24	Over 65 years n = 8	P value[1] M vs F
Dermoscopic features			
Gray color	14 (58.3%)	8 (100.0%)	0.035*
Asymmetric pigmented follicular openings	18 (75.0%)	5 (62.5%)	0.820
Annular granular pattern	7 (29.2%)	1 (12.5%)	0.637
Circle within a circle	2 (8.3%)	0 (0.0%)	1.000*
Pigmented rhomboidal structures	14 (58.3%)	1 (12.5%)	0.041*
Darkening at dermoscopic examination	0 (0.0%)	0 (0.0%)	
Target-like pattern	0 (0.0%)	1 (12.5%)	0.557
Increased density of vascular network	3 (12.5%)	3 (37.5%)	0.148*
Red rhomboidal structures	2 (8.3%)	0 (0.0%)	1.000*
Obliterated hair follicles	5 (20.8%)	3 (37.5%)	0.637
White scar-like areas	3 (12.5%)	5 (62.5%)	0.012*
Globules/dots	5 (20.8%)	2 (25.0%)	1.000*

*Fisher exact test

[1]Chi-squared test

M, Male; LM, lentigo maligna; F, female. n, absolute number

DISCUSSION

LM represents an *in situ* melanoma that develops on chronically photo-damaged skin, and which, when progresses to an invasive form, exhibits the same biological aggressiveness as other forms of melanoma. Clinical diagnosis of LM is often difficult, even for educated and experienced dermatologists specializing in early detection of malignant skin tumors. The reason for this is the existence of numerous pigmentary lesions that also occur on chronically photo-damaged skin, such as solar lentigo, flat seborrheic keratosis, lichen planus-like keratosis or melanocytic nevus. Due to the difficulty in diagnosing and features overlapping with other changes, findings regarding the potential influence of age, gender and topography on the clinical and dermoscopic presentation of LM can be of great significance in everyday clinical practice (8 - 9).

LM is most commonly found in individuals over 50 years of age, with an average patient age of 67.5 years (7 - 9), which is consistent with the results of this study. Specifically, in our study, the average age of patients with LM was 60.1 ± 10.4 years, with the youngest patient being 34 years old and the oldest one being 80 years old.

Contradictory data regarding the prevalence of LM in males and females are encountered in the literature. In certain studies, LM is more frequent in males, while in others, it is more frequent in females (15 - 17). In the conducted study, a slightly higher prevalence of LM was observed in male participants (59.4%). Some studies indicate that gender differences influence the risk of developing melanoma as well as the prognosis of the disease itself. A stronger correlation between UV index and male gender was observed. Differences in behavior exist as well, such as the fact that women tend to visit a doctor earlier for the examination of suspicious skin changes or work indoors more frequently compared to men. Exactly these reasons are considered to be responsible for a better prognosis of melanoma in female patients (18).

LM is more frequently localized on the head and neck compared to the other types of *in situ* melanoma. In the study conducted by Higgins et al., it was observed that LM was most frequently localized on the head and neck region in both genders (18). In this study, LM was also most commonly localized on the skin of the head and neck, which is consistent with the literature data. Specifically, 28 LM cases (87.5%) were localized on the skin of the head, whereas 4 LM cases (12.5%) had extrafacial localization which included the skin of the lower leg, back and neck. In the aforementioned study by Higgins et al., the trunk was the most common localization of LM after the head and neck region in males (18). In our study, which involved a smaller number of patients compared to the study conducted by Higgins et al., out of four cases of extrafacial LM, one male had LM on the skin of the trunk, and one female had LM on the skin of the lower leg, which is in line with the literature data supporting the predominance of extrafacial localization of LM on the trunk skin in males and on the lower leg skin in females.

With regard to the localization of LM on the facial skin, cheeks were by far the most common LM site with 13 cases (40.6%), followed by localization on the skin of the ear (12.5%) and nose (12.5%). The results of this study are consistent with a multicentric study that examined the anatomical localization of LM. In that study, which included 201 cases of LM in 200 patients from 2012 to 2013 in four academic centers in France, Italy, Serbia and the United States, localization of LM on the skin of the cheeks was observed in 108 patients (53.7%), while LM was found on the skin of the ear in 10 patients (10%) and on the skin of the nose in 15% (67) (14). This study also revealed certain differences in gender distribution related to the anatomical localization of LM. While no predominant anatomical localization for LM was observed in males, the dominant localization of LM in females was on the skin of the cheeks (69.2%). It was determined that there was a statistically significant difference in the frequency of LM localized on the cheeks in relation to gender. The results are consistent with the results in the literature, where the localization on the skin of the cheeks is significantly more common in females than in males (14).

In our study, a difference in the anatomical localization of LM was observed depending on the age of the patient. In the group of patients younger than 65 years, LM was most frequently diagnosed on the skin of the cheeks and ears, while the nose and cheeks were the most common localizations of LM in patients older than 65 years. These results could not be compared with the literature data, as there are no published results that compared the age of the participants with the anatomical localization of LM. *in situ* lesions was determined. Specifically, all le-

sions were divided into the lesions larger than 10 mm and those smaller than 10 mm. LM larger than 10 mm was found in 56.3% of patients, while LM smaller than 10 mm was observed in 18 patients or 43.8%. No difference in gender distribution and LM size was observed. LM larger than 10 mm was present in just over half of the participants, i.e. 56.3%. These data show that almost half of the diagnosed cases of LM in our study were smaller than 1 cm, indicating very small lesions. Similar results were shown in the study conducted by Zalaudek et al., in which 51.2% of LM lesions were smaller than 10 mm (14). These results not only refute the common belief that LM is clinically manifested as larger pigmented lesions, but also indicate that this malignant tumor can be present in the form of a pigmented lesion of smaller dimensions. This finding has clinical significance and emphasizes the need for equally detailed clinical and dermoscopic examination of smaller pigmented lesions.

The main dermoscopic features of LM include asymmetric follicular openings, of annular-granular pattern, pigmented rhomboidal structures, circles within circles, obliterated hair follicles, white scar-like areas. Recently, additional dermoscopic features of LM have been described, including brown dots within black circles called target-like structures, increased density of vascular network, darkening at dermoscopic examination, as well as the presence of globules and dots (10 - 14). However, in its earliest stage, LM may exhibit only a few non-specific dermoscopic features, and sometimes the presence of only a gray color can be the key factor in decision for excision.

In our study, the most frequent dermoscopic features of the examined LMs were asymmetric follicular openings (71.9%), gray color (68.8%) and pigmented rhomboidal structures (46.9%). These results are consistent with the literature data, where asymmetric pigmented follicular openings, dark rhomboidal structures and grayish areas are considered dermoscopic features with high sensitivity and specificity for LM diagnosis (10 - 14).

In the conducted study, the distribution of dermoscopic features was consistent with respect to gender. Thus, gray color (73.7%) and asymmetric follicular openings (57.9%) represented the most commonly observed dermoscopic features of LM in males, while asymmetric follicular openings (92.3%) and gray color (61.5%) were the most common ones in females. Gray color was not only one of the most prevalent dermoscopic features in the examined LM series, but it was also statistically significantly more common in the group of older patients (100.0% vs. 58.3%, $p = 0.035$). These results are in correlation with the results of the conducted multicentric study, where gray color was the most common dermoscopic feature, observed in 178 cases of LM (88.6%) (14).

Pigmented rhomboidal structures were the third most frequent dermoscopic feature of LM (46.9%), and they were more frequently observed in the group of younger patients (58.3% vs. 12.5%, $p = 0.041$). Rhomboidal structures represent the dermoscopic criterion most frequently present in most studies, with an incidence ranging from 56% to 75%. In a retrospective study published by Lallas et al., it was observed that gray rhomboidal lines were the most common predictor for LM, and their presence increased the likelihood of LM diagnosis six times (19).

Unlike pigmented rhomboidal structures, white scar-like areas were detected in the group of older patients (62.5% vs. 12.5%, $p = 0.012$). It is known that rhomboidal structures are a dermoscopic criterion that can be detected at the very beginning of LM, therefore, they may occur at a younger age as well. With age, LM slowly progresses further with the appearance of other dermoscopic features representing a more invasive form of LM, thus a higher prevalence of white scar-like areas is detected in older patients. The presence of different dermoscopic features reflects the progressive model of LM from an early non-invasive stage to a more invasive form and progression to LMM (10-14, 19).

CONCLUSION

The observed differences in the frequency of clinical and dermoscopic features of LM have significant clinical importance in everyday clinical practice and can assist clinicians in the early diagnosis of this malignant tumor.

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Kliničke i dermoskopske karakteristike lentigo maligna

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SAŽETAK

Uvod/Cilj. Lentigo maligna (LM) predstavlja *in situ* melanom koji se razvija na hronično fotooštećenoj koži. Klinička dijagnoza LM-a često je teška, čak i za iskusnog dermatologa. Cilj ovog rada bila je analiza kliničkih i dermoskopskih karakteristika kod bolesnika sa patohistološki potvrđenom dijagnozom LM-a, kao i ispitivanje mogućeg uticaja anatomske lokalizacije, starosti i pola na dermoskopske odlike LM-a.
Bolesnici i metode. Retrospektivnom studijom obuhvaćeno je 32 bolesnika sa ukupno 32 LM-a, dijagnostikovana u periodu od 2017. do 2020. godine. Klinički podaci uzeti od svakog bolesnika obuhvatili su demografske karakterstike (starost i pol), anatomsku lokalizaciju (facijalnu i ekstrafacijalnu) i kliničku veličinu promene (< 10 mm ili > 10 mm). Facijalna regija naknadno je podeljena na osam različitih topografskih područja, dok je ekstrafacijalna lokalizacija podrazumevala bilo koju regiju tela sem facijalne. Sve dermoskopske slike analizirane su na prisustvo dermoskopskih karakteristika prethodno opisanih za LM.
Rezultati. Od ukupno 32 ispitanika, njih 19 bilo je muškog, a njih 13 ženskog pola. Starost bolesnika kretala se od 34 do 80 godina (prosečna starost bila je 61 ± 10,4 godine). Kod žena je lokalizacija na obrazima bila statistički zastupljenija nego kod muškaraca (p = 0,018). Lokalizacija na nosu bila je signifikatno povezana sa bolesnicima starijim od 65 godina (p = 0,039). Najčešće dermoskopske karakteristike bile su: asimetrični folikularni otvori – 23 (71,9%), siva boja – 22 (68,8%), pigmentne romboidne strukture – 15 (46,9%). Kada je reč o starosti i specifičnim dermoskopskim karakteristikama, zapaženo je da su siva boja (p = 0,035) i bela područja nalik na ožiljak (p = 0,012) bila signifikantno zastupljenija kod bolesnika starijih od 65 godina, kao i da su pigmentne romboidne strukture (p = 0,041) bile značajno više zastupljene kod mlađih bolesnika.
Zaključak. Uočene razlike u učestalosti kliničkih i dermoskopskih karakteristika LM-a imaju veliki značaj u svakodnevnom kliničkom radu i mogu pomoći kliničaru u ranoj dijagnozi ovog malignog tumora.

Ključne reči: **lentigo maligna, dermoskopija, diferencijalna dijagnoza**