





Dermoscopy of atypical pigmented lesions of the face: Variation according to facial areas

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Abstract

Atypical pigmented facial lesions (aPFLs)—including lentigo maligna (LM) and lentigo maligna melanoma (LMM), solar lentigo (SL), pigmented actinic keratosis (PAK), atypical nevi (AN), seborrheic keratosis (SK) and lichen planus-like keratosis (LPLK)—can exhibit clinical and dermoscopic overlapping features. We aimed to investigate if and

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how 14 dermoscopic features suggestive for the aforementioned aPFLs vary according to six facial sites among 1197 aPFLs cases (excised to rule out malignancy) along with lesion and patients' metadata. According to distribution and association analysis, aPFLs on the forehead of a male patient aged > 69 years displaying the *obliterated follicular openings* pattern, appear to be more at risk of malignancy. Of converse, aPFLs of the orbital/cheek/nose area with evident and regular follicular openings with diameter < 10 mm in a female aged below 68 are probably benign. The *obliterated follicular openings*, *keratin plugs*, *evident and regular follicular openings* and *target-like pattern* features differed significantly among six facial areas in all aPFLs cases. Lesion of the nose may show both features suggestive of malignancy and benignity (e.g. many SL and PAK may display *target-like pattern* and some LM/LMM cases display *keratin plugs* and *evident and follicular openings*), making these features less specific.

KEYWORDS

atypical pigmented facial lesions, dermoscopy, facial areas, lentigo maligna melanoma, registry

1 | BACKGROUND

In the last decades, an increasing trend for pigmented facial lesions development has been documented: progressive population ageing and inappropriate sun exposure habits has been indicated as possible contributing factors.¹⁻³ Then, the differential diagnosis between benign and malignant aPFLs, especially when the lesions develop on mottled chronic sun-damaged skin and/or when they display atypical appearance, can be challenging.^{4,5} Indeed, some benign pigmented facial lesions may exhibit under the dermatoscope similar features to malignant lesions. From a clinico-dermoscopic point of view, these lesions are collectively referred to as atypical pigmented facial lesions (aPFLs),⁴⁻⁶ and include lentigo maligna (LM), lentigo maligna melanoma (LMM), pigmented actinic keratosis (PAK), solar lentigo (SL), benign lichenoid keratosis (BLK), flat seborrheic keratosis (SK) and flat atypical nevi (AN). Still, although the dermoscopic features of facial pigmented lesions have been widely described in the last 20 years, the current dermoscopic knowledge of pattern analysis is not accurate enough to distinguish LMM from benign/premalignant aPFLs in equivocal cases (i.e. ~41% accuracy).⁷ Thus, skin biopsy is required. Moreover, it has not been elucidated yet, if a particular localization within the facial surface can impact the dermoscopic presentation of a pigmented lesion, as it was demonstrated for atypical melanocytic lesions on the body.⁸ On the face, the pseudo-network pattern may actually occur both in melanocytic and in non-melanocytic lesions, which further complicates the differential diagnosis.

2 | QUESTIONS ADDRESSED

Having this in mind, we aimed to investigate if and how a pool of relevant dermoscopic features suggestive of the seven aforementioned

aPFLs could vary according to the specific facial areas, and if there were significant differences among benign and malignant aPFLs.

3 | EXPERIMENTAL DESIGN

We previously set up a registry (the *iDScore facial dataset*) of 1197 aPFL cases excised with a clinical suspicion of malignancy, all having the dermoscopic pictures integrated with the clinical data.³ Each case was composed of a standardized dermoscopic image (clinical pictures were additionally available in 60% of cases) and four objective data: maximum diameter (mm), age (years), sex (male/female) and facial site. The face was divided into a 6-area—orbital area, forehead, nose, cheek, chin, mouth area—classification (Figure 1) by taking into account both skin morphology, aesthetics and anatomical features, as routinely done in plastic surgery.⁵ The mouth area included the skin around the lips and the vermilion site, but excluded the labial semi-mucosa, due to different dermoscopic patterns. Similarly, the orbital area included the eyelid and the surrounding skin, but not the conjunctiva, and the nose area did not include the nasal mucosa. Pattern analysis was performed by either dermatologists ($n=102$) or dermatology residents ($n=52$) through an online tele-dermoscopic test specifically designed and hosted on a dedicated web platform (i.e. *iDScore facial project*, <https://en.idscore.net/projects/facial-lesions/facial-lesions-2021>).^{3,4} Based on self-assessment, the evaluators declared different levels of experience in dermoscopy, that is, <1 year ($n=34$), 1-4 years ($n=44$), 5-8 years ($n=22$) and >8 years ($n=54$).⁴ The pattern analysis relied on recognition of presence/absence of a series of 14 dermoscopic features in each dermoscopic photo. Based on literature consensus, the 14 dermoscopic features had been previously selected as most representative for each aPFL (Table 1).^{6,7} Each lesion was assessed by two to four evaluators. If one out of two, two out of three or three out of four evaluators were

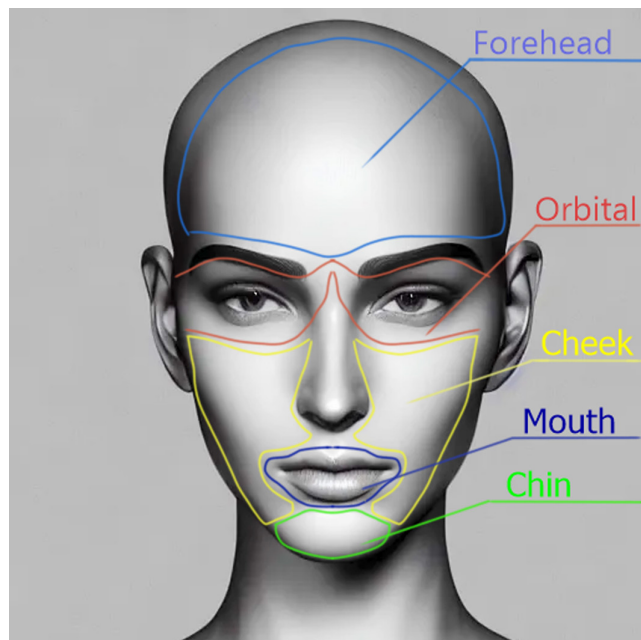


FIGURE 1 Schematic representation of the six facial areas examined in the study.

in accordance, the pattern was considered to be present/absent in a specific lesion.

4 | RESULTS

Descriptive statistics and univariate association analysis of dermoscopic pattern and lesions and patients' metadata were carried out according to data distribution among the six facial areas (Table 1). Most aPFLs were located on the cheek ($n=595$;50%), followed by the forehead ($n=216$;18%) and nose ($n=200$, 11%). The eldest patients had aPFLs of the mouth (72.2 years on average) while a prevalence of phototype III patients had lesions located on the cheek: both parameters did not vary significantly among facial areas. Instead, the factor male sex was more prevalent in the group of forehead lesions than the female sex ($p<0.001$). Maximum diameter variation among subareas was not statistically significant, as the range was 9.61–11.7 mm, with the higher value in chin lesions.

Concerning dermoscopic pattern distribution and association analysis of all aPFLs cases, a total of four dermoscopic features turned out to vary significantly among facial areas ($p<0.05$), namely: the *obliterated follicular openings*, the *keratin plugs* and the *evident, the regular follicular openings* and the *target-like pattern*. In particular, the *obliterated follicular openings* was significantly more prevalent in the forehead than in the mouth and chin, the *keratin plug* were significantly more prevalent in the nose than in other areas, the *evident and regular follicular openings* were significantly more prevalent in the nose than in cheek, orbital area, forehead and chin, the *target-like pattern* was significantly more prevalent in the nose than in the orbital area and the cheek. Figure 2 illustrates six exemplificative cases of aPFLs (clinical and dermoscopic image, polarized light) illustrating

the most significant associations of between a dermoscopic pattern and a specific facial location emerged from the statistical analysis of the study.

A sub-analysis of dermoscopic pattern distribution and association according to benignity/malignancy criteria (Table 1) revealed that only three features significantly varied among facial areas in malignant cases (*obliterated follicular openings*, *keratin plugs*, *evident and regular follicular openings*) while only two features significantly varied in benign cases (*keratin plugs*, *evident and regular follicular openings*). In the malignant aPFLs group (LM+LMM), the *obliterated follicular openings* were observed predominantly in the forehead than the cheek and nose, the *keratin plugs* in the nose than in cheek, forehead and orbital area, the *evident and regular follicular openings* in the nose than in chin and cheek. Of note, in benign lesions, the rates of recognition of the *obliterated follicular openings* pattern were generally inferior than in malignant ones, while the recognition of *evident and regular follicular openings* and *keratin plug* feature was generally superior. The *target-like pattern* distribution did not reach a statistically significant variation in this sub-analysis due to the inferior numerosity of location subgroups within each dataset of malignant/benign cases.

Finally, the sub-analysis of lesions/patients' metadata showed that age ($p=0.005$) and sex ($p=0.016$) significantly varied from benign to malignant groups. In particular, patients with LM/LMM were older than patients with benign aPFLs (69.55 ± 12.94 vs. 63.23 ± 14.26 years on average) and there were more male patients than females (46% vs. 39%) in the malignant group.

5 | CONCLUSIONS AND PERSPECTIVES

Since the progressive diffusion of dermoscopic examination of pigmented lesion of the face in 2000, a series of dermoscopic patterns have been distinguished as suggestive for LM, namely: *hyperpigmented follicular openings*, *target-like pattern*, *obliterated follicular openings*, *polygonal structures*. Recently, it has been argued that the same dermoscopic features can be observed in benign aPFLs.^{4,6–8} Subsequently, an inverse approach, based on the identification of definitely benign dermoscopic patterns, that is, *evident and regular follicular openings*, *keratin plugs*, *light brown fingerprint*, *diffuse opaque light brown pigmentation* and *comedo-like openings*, was also suggested.⁹ However, no study to date has investigated the distribution of these patterns according to the face area. In the current study, a large dataset analysis of benign and malignant aPFLs was investigated to derive new insights concerning the distribution among facial areas of both patients' and lesions' metadata with dermoscopic pattern data namely: descriptive and association data in all cases and in histologically defined groups to assess significant differences.

First, we found that a male patients aged >69 years, phototype III exhibiting an aPFLs of the forehead or chin with ≥ 11 mm in diameter has more possibility to have a malignant than a benign lesion.

Second, four dermoscopic features (i.e. *obliterated follicular openings*, *target-like pattern*, *keratin plugs*, *evident and regular follicular*

TABLE 1 Descriptive statistics, distribution analysis (*p*) and paired association analysis (*) between 14 dermoscopic patterns and 6 facial areas, assessed in 1197 atypical pigmented facial lesions (aPFLs).

	Orbital area	Forehead	Nose	Cheek	Chin	Mouth	<i>p</i>
All aPFLs [n(%)]							
Patient age	63.7 (14.15)	66.7 (14.36)	66.9 (13.09)	64.8 (14.52)	63.8 (14.58)	72.2 (12.14)	0.057
Patient sex (male)	52 (40.3)	139 (64.4)	95 (47.5)	272 (45.7)	17 (43.6)	5 (29.4)	<0.001
Lesion maximum diameter (mean, SD)	10.4 (5.5)	10.9 (8)	9.6 (7.9)	10.4 (6.5)	11.7 (10.9)	9.61 (6.7)	0.447
Phototype							
I	0 (0.0)	1 (1.1)	2 (2.8)	2 (0.8)	0 (0.0)	0 (0.0)	0.825
II	20 (38.5)	28 (30.8)	30 (42.3)	111 (41.7)	3 (30.0)	2 (33.3)	
III	32 (61.5)	62 (68.1)	38 (53.5)	150 (56.4)	7 (70.0)	4 (66.7)	
IV	0 (0.0)	0 (0.0)	1 (1.4)	3 (1.1)	0 (0.0)	0 (0.0)	
14 Dermoscopic features							
Hyperpigmented follicular openings	41 (31.8)	87 (40.3)	95 (47.5)	236 (39.7)	16 (41.1)	10 (55.6)	0.075
Target-like pattern	12 (9.3)	33 (15.3)	46 (23.0)	82 (13.8)	7 (17.9)	5 (27.8)	0.007^{a,b}
Annular-granular pattern	51 (39.5)	68 (31.5)	62 (31.0)	217 (36.5)	12 (30.8)	5 (27.8)	0.416
Pigment rhomboids/polygons	33 (25.6)	61 (28.2)	63 (31.5)	168 (28.2)	12 (30.8)	4 (22.2)	0.863
Obliterated follicular openings	27 (20.9)	73 (33.8)	35 (17.5)	131 (22.0)	12 (30.8)	3 (16.7)	0.002^{c,f}
Red structures and lines	23 (17.8)	32 (14.8)	44 (22.0)	117 (19.7)	5 (12.8)	5 (27.8)	0.326
Keratin plugs	16 (12.4)	44 (20.4)	76 (38.0)	130 (21.8)	5 (12.8)	6 (33.3)	<0.001^{a,b,c,d,e}
Light brown fingerprint-like structures/areas	24 (18.6)	46 (21.3)	31 (15.5)	100 (16.8)	12 (30.8)	2 (11.1)	0.159
Moth-eaten borders	30 (23.3)	53 (24.5)	58 (29.0)	144 (24.2)	12 (30.8)	2 (11.1)	0.455
Diffuse opaque yellow-brown pigmentation	36 (27.9)	58 (26.9)	60 (30.0)	167 (28.1)	13 (33.3)	9 (50.0)	0.406
Fat fingers	12 (9.3)	14 (6.5)	11 (5.5)	46 (7.7)	3 (7.7)	1 (5.6)	0.821
Milia-like cysts	11 (8.5)	24 (11.1)	17 (8.5)	50 (8.4)	3 (7.7)	1 (5.6)	0.867
Comedo-like openings	14 (10.9)	25 (11.6)	25 (12.5)	51 (8.6)	4 (10.3)	3 (16.7)	0.520
Evident and regular follicular openings	57 (44.2)	83 (38.4)	120 (60.0)	259 (43.5)	13 (33.3)	8 (44.4)	<0.001^{a,b,c,d}
Malignant aPFLs [n(%)]							
14 Dermoscopic features							
Hyperpigmented follicular openings	27 (54.0)	49 (56.3)	57 (62.6)	141 (56.9)	7 (50)	7 (77.8)	0.676
Target-like pattern	10 (20.0)	19 (21.8)	32 (35.2)	55 (22.2)	4 (28.6)	4 (44.4)	0.104
Annular-granular pattern	22 (44.0)	32 (36.8)	30 (33.0)	115 (46.4)	6 (42.9)	3 (33.3)	0.276
Pigment rhomboids/polygons	23 (46.0)	40 (46.0)	45 (49.5)	112 (45.2)	6 (42.9)	3 (33.3)	0.950
Obliterated follicular openings	21 (42.0)	46 (52.9)	24 (26.4)	87 (35.1)	7 (50.0)	3 (33.3)	0.008^{c,f}
Red structures and lines	7 (14.0)	9 (10.3)	19 (20.9)	54 (21.8)	1 (7.1)	3 (33.3)	0.106
Keratin plugs	6 (12.0)	15 (17.2)	36 (39.6)	53 (21.4)	2 (14.3)	4 (44.4)	<0.001^{a,b,c}
Light brown fingerprint-like structures/areas	8 (16.0)	20 (23.0)	15 (16.5)	30 (12.1)	3 (21.4)	2 (22.2)	0.250
Moth-eaten borders	11 (22.0)	17 (19.5)	23 (25.3)	44 (17.7)	3 (21.4)	1 (11.1)	0.703

(Continues)

TABLE 1 (Continued)

	Orbital area	Forehead	Nose	Cheek	Chin	Mouth	<i>p</i>
Diffuse opaque yellow-brown pigmentation	9 (18.0)	20 (23.0)	25 (27.5)	48 (19.4)	1 (7.1)	3 (33.3)	0.351
Fat fingers	3 (6.0)	3 (3.4)	6 (6.6)	14 (5.6)	1 (7.1)	0 (0.0)	0.906
Milia-like cysts	6 (12.0)	8 (9.2)	8 (8.8)	14 (5.6)	1 (7.1)	0 (0.0)	0.544
Comedo-like openings	8 (16.0)	8 (9.2)	14 (15.4)	17 (6.9)	1 (7.1)	2 (22.2)	0.097
Evident and regular follicular openings	18 (36.0)	24 (27.6)	46 (50.5)	86 (34.7)	1 (7.1)	4 (44.4)	0.005^{c,d}
Benign aPFLs [n(%)]							
14 Dermoscopic features	79 (6.5)	129 (10)	109 (9)	347 (28)	25 (2)	9 (0.7)	
Hyperpigmented follicular openings	14 (17.7)	38 (29.5)	38 (34.9)	95 (27.4)	9 (36.0)	3 (33.3)	0.170
Target-like pattern	2 (2.5)	14 (10.9)	14 (12.8)	27 (7.8)	3 (12.0)	1 (11.1)	0.177
Annular-granular pattern	29 (36.7)	36 (27.9)	32 (29.4)	102 (29.4)	6 (24.0)	2 (22.2)	0.744
Pigment rhomboids/polygons	10 (12.7)	21 (16.3)	18 (16.5)	56 (16.1)	6 (24.0)	1 (11.1)	0.844
Obliterated follicular openings	6 (7.6)	27 (20.9)	11 (10.1)	44 (12.7)	5 (20.0)	0 (0.0)	0.033
Red structures and lines	16 (20.3)	23 (17.8)	25 (22.9)	63 (18.2)	4 (16.0)	2 (22.2)	0.894
Keratin plugs	10 (12.7)	29 (22.5)	40 (36.7)	77 (22.2)	3 (12.0)	2 (22.2)	0.003^{a,b}
Light brown fingerprint-like structures/areas	16 (20.3)	26 (20.2)	16 (14.7)	70 (20.2)	9 (36.0)	0 (0.0)	0.143
Moth-eaten borders	19 (24.1)	36 (27.9)	35 (32.1)	100 (28.8)	9 (36.0)	1 (11.1)	0.622
Diffuse opaque yellow-brown pigmentation	27 (34.2)	38 (29.5)	35 (32.1)	119 (34.3)	12 (48.0)	6 (66.7)	0.165
Fat fingers	9 (11.4)	11 (8.5)	5 (4.6)	32 (9.2)	2 (8.0)	1 (11.1)	0.658
Milia-like cysts	5 (6.3)	16 (12.4)	9 (8.3)	36 (10.4)	2 (8.0)	1 (11.1)	0.766
Comedo-like openings	6 (7.6)	17 (13.2)	11 (10.1)	34 (9.8)	3 (12.0)	1 (11.1)	0.854
Evident and regular follicular openings	39 (49.4)	59 (45.7)	74 (67.9)	173 (49.9)	12 (48.0)	4 (44.4)	0.014^{b,c}

Note: The following paired comparisons are statistically different: (a) nose–orbital area; (b) nose–cheek; (c) nose–forehead; (d) nose–chin; (e) cheek–orbital; (f) cheek–forehead.

Values in bold had a significance of <0.05.

openings) seem to vary significantly in frequency through facial areas in aPFLs. The specific prevalence rates here found can be explained both by structural skin differences between facial areas and by the histology of the lesion itself. Most of all, the nasal area turned out to be particularly challenging. Indeed, the nose hosted a quote of LM/LMM cases (499) showing also benign-orienting feature, namely the *evident and regular follicular openings* (46 cases) and *keratin plugs* (36 cases): this appearance may be explained by the peculiar anatomy of nasal skin. On the other hand, 14 benign cases exhibited the *target-like pattern* in the nose area. Moreover, the keratin plugs pattern was mostly encountered on the forehead/cheek/nose areas, as expression of the prevalence of sun-induced PAK lesions in these areas. Then, the *pigment rhomboids/polygons* feature was more frequently recognized in malignant lesions, but without a site-specific predominance; of converse, the diffuse opaque yellow-brown pigmentation and the light brown fingerprint-like structures/areas features were more frequently recognized in benign lesion, similarly among facial areas.

Third, we found that two association among a specific dermoscopic pattern and a facial area were significantly different in benign and malignant lesions groups, that is, (a) the *obliterated follicular openings pattern* was present in 53% and 50% of LM/LMM cases of the forehead and chin, respectively, resulting to be a potential marker of malignancy at these sites ($p=0.008$); (b) the *evident and regular follicular openings* pattern was present in 68%, 50% and 49% of benign aPFLs cases of the nose, cheek and orbital area, resulting to be a potential marker of benignity at these sites ($p=0.014$); this distribution can also be ascribed to the relevant quote of SL cases at the aforementioned sites, induced by UV-rays. Fourth, the *keratin plug* and *target-like pattern*, which were traditionally considered as suggestive of a benignity and malignancy, respectively, in clear-cut cases, here in this dermoscopic analysis of only challenging aPFLs resulted to be less specific than the previously aforementioned features and particularly they can be found in both benign and malignant lesions of the nasal area. Indeed, the

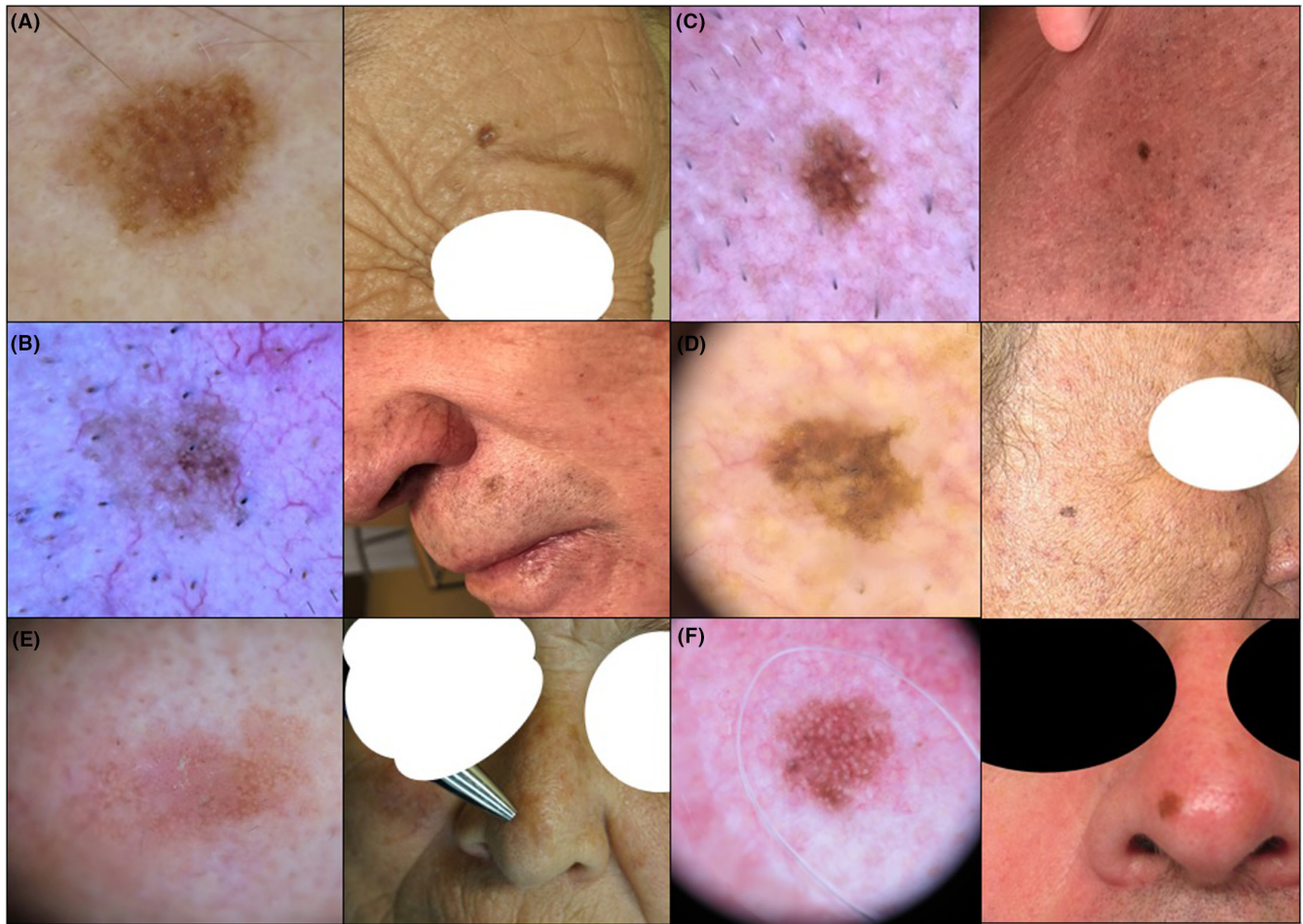


FIGURE 2 Exemplificative cases of atypical pigmented lesions (clinical and dermoscopic image, polarized light) illustrating the most significant associations of between a dermoscopic pattern and a specific facial location emerged from the statistical analysis of the study: presence of the *obliterated follicular openings* pattern in lentigo maligna of the forehead (A, female, 68 years, 6 mm) and mouth (B, male, 75 years, 6 mm); of the *evident and regular follicular openings* pattern in atypical nevus of the cheek (C, male, 62 years, 3 mm) and in a solar lentigo of the orbital area (D, male, 76 years, 5 mm); presence of *keratin plugs* in a pigmented actinic keratosis of the nose (E, female, 75 years, 5 mm) and of *target-like pattern* in a lentigo maligna of the nose (F, male, 70 years, 6 mm).

target-like pattern and the *keratin plug* pattern were significantly more prevalent on the nose ($p=0.007$ and $p<0.001$, respectively) only in all aPFLs analysis, but not when analysing the benign and malignant group separately.

Summarizing, the present findings demonstrate that the traditionally recognized dermoscopic patterns are generally poorly specific of malignancy/benignity when dealing with difficult equivocal aPFLs and that a site specific variation can be due to both skin anatomy (e.g. nose) and photoexposure entity (forehead, cheek).^{4,8,10} The nasal area turned out to be particularly challenging. In conclusion, dermatologists should pay particular attention to aPFLs, especially in male patients aged >69 years, lesions located on the forehead area displaying the *obliterated follicular openings* pattern, as well as an aPFL at any facial area with pigment rhomboids and a diameter >11 mm, especially in a male. Of converse, the presence of an aPFLs of the orbital area, cheek and nose with evident and regular follicular openings with diameter <10 mm in a female aged

below 69 is probably benign, as well as an aPFL at any facial site showing both *light brown fingerprint-like structures/areas* and *diffuse opaque yellow-brown pigmentation*, especially in women.

In the nasal area, dermatologists should keep in mind that some benign aPFLs (SL, PAK) can exhibit *target-like pattern* and that some LM can display also *keratin plugs* and/or *evident and follicular openings* are also observable. Finally, given the increasing number of patients with important facial photodamage, it could be advisable that each dermatology residency program include a specific dermoscopic training for facial pigmented lesions.

AUTHOR CONTRIBUTIONS

LT, EC, EM, ED, FF, JP, AL, DT, IS, CL, MS, IZ, GA and JLP contributed to data collection. MZ, SG, GR and PR contributed to data analysis. AC, MD, GC and LT performed the statistical analysis. LT, AC, EC and PR designed the research study. LT, AC and MD wrote the paper. EC, MR, MZ and EM revised the paper.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

INFORMED CONSENT

The patients in this manuscript have given written informed consent to publication of their case details.

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