Pigmented Macules on the Head and Neck: A Systematic Review of Dermoscopy Features

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Introduction: Differentiating early melanoma from other flat pigmented lesions on the head and neck is challenging both clinically and dermoscopically, partly due to the wide differential diagnosis and the lack of specific diagnostic algorithms.

Objectives: To review publications covering the dermoscopic features of pigmented macules on the head and neck.

Methods: Embase and PubMed (Medline) database from January 2015 to January 2021 were searched using a four-step search. Keywords used were dermoscopy/dermatoscopy or epiluminescence microscopy, lentigo maligna, lentigo maligna melanoma, lichen-planus-like-keratosis, solar lentigo, seborrheic keratosis, pigmented actinic keratosis (PAK), pigmented Bowen disease (pBD), pigmented intraepidermal carcinoma (pIEC) and head and neck.

Results: The commonest reported dermoscopic features of facial melanoma were irregular dots, atypical dots/globules, asymmetric pigmented follicular openings, rhomboid gray/black structures, increased vascular network, brown globules/dots and a pattern of circles. Pseudopods, radial streaming, blue white veil, irregular blotches, scar-like depigmentation and atypical pigment network were recorded in low frequencies. For PAK, pBD and pIEC perifollicular erythema, white/yellow surface scale, linear wavy vessels around hair follicles, hair follicular openings surrounded by a white halo, evident follicles or follicular or keratotic plugs, rosette sign and sharply demarcated borders were the salient features.

Conclusions: Further studies are needed to determine the dermoscopic criteria for pigmented melanocytic and non-melanocytic lesions on the head and neck. Furthermore, there is a gap in the knowledge of site-specific dermoscopic features on specific sites, namely ears, nose, cheeks, scalp and neck which will also benefit from further studies.

ABSTRACT
Introduction

Melanoma diagnosis on chronic sun-damaged skin is challenging to clinicians both clinically and dermoscopically [1-5]. This is partly due to the overlap of melanoma (Figure 1) features with non-melanoma skin lesions including solar lentigo (SL) (Figure 2), seborrhoeic keratosis (SK) (Figure 3), pigmented actinic keratosis (PAK)/ pigmented Bowen disease (pBD)/ pigmented intraepidermal carcinoma (pIEC) (Figures 4 and 6) and lichen planus like keratosis.

Figure 1. (A) Macroscopy of a pigmented lesion on the scalp (vertex) of a 49-year-old male. (B) Dermoscopy features of the lesion showing brown and gray structureless areas (oval shape), gray structureless areas (hollow arrows), white regression areas (solid black arrow) and brown dots/globules (orange solid arrow)-Fotofinder dermoscopy, Medicam 1000, magnification x20. Diagnosis: melanoma in situ (lentigo maligna). (C)Macroscopy of a pigmented lesion on the left cheek of a 69-year-old male with a long standing “freckle” on his left cheek. (D) Dermoscopy features of the lesion showing a pattern of circles with multiple asymmetrically pigmented hair follicles (round shape), circle in circle (solid arrow), target shapes (hollow arrows), erythema/ structureless pink areas (black oval shape) and gray areas (blue oval shape)-Fotofinder dermoscopy, Medicam 1000, magnification x20. Diagnosis: melanoma in situ (lentigo maligna). (E) Macroscopy of a pigmented lesion on the right cheek of a 70-year-old male. (F) Dermoscopy features of the lesion showing a pattern of gray-brown granules/ peppering (round shapes), asymmetrically pigmented follicular opening (arrow) and brown-black areas (oval shape)-Fotofinder dermoscopy, Medicam 1000, magnification x20. Diagnosis: melanoma in situ (lentigo maligna).
Compared to other parts of the body, the head and neck region has features of sun-damage, increased elastosis, increased intensity of hair follicular openings and skin appendages as well as flat rete ridges creating a pseudo-pigment network. These collectively can render the extra-facial diagnostic algorithms for melanoma diagnosis unreliable. Furthermore, prior therapeutic interventions like cryosurgery, curettage/electrodesiccation as well as topical treatment may result in scarring and hypopigmentation adding to the diagnostic difficulty.

Approximately 20% of melanomas occur on the head and neck [7]. The estimated five year survival rate on the head and neck is lower (74%) compared to melanoma located on the extremities (84%) and trunk (82%) [8,9].
Figure 4. (A) Macroscopy - A 50-year-old female with a lesion on the left cheek. (B) Dermoscopy - Diagnosis: pigmented actinic keratosis. (C) Macroscopy - A 67-year-old male with a pigmented lesion on the right eyebrow. (D) Dermoscopy - Diagnosis: pigmented Bowen disease. (E) Macroscopy - A 33-year-old female with a left cheek lesion. (F) Dermoscopy - Diagnosis: pigmented intraepidermal carcinoma. Fotofinder dermoscopy, Medicam 1000, magnification x20.

Figure 5. Macroscopy - Left side - A 71-year-old male with a pigmented lesion on the left side of the forehead with peppering or annular granular structures composed of scattered dots of gray pigmentation all over the lesion. Dermoscopy - Right side - Diagnosis: lichen planus like keratosis. Fotofinder dermoscopy, Medicam 1000, magnification x20.
Lentigo maligna (LM), formerly known as Hutchinson melanotic freckle (HMF) is the commonest type of in situ melanoma on sun-exposed areas [10]. It tends to develop clinically as a brown macule on chronic sun-exposed sites. Dermoscopically the differential diagnosis is variable and the clinical and dermoscopic margins tend to be ill-defined which can lead to incomplete excisions [11]. Progression to an invasive stage is called lentigo maligna melanoma (LMM) which represents 4%-15% of all invasive melanomas [12]. Estimations of lifetime risk of LM progressing into LMM is 5%-20% [11].

Dermoscopy is a non-invasive technique that increases the diagnostic accuracy of skin lesions. In expert hands diagnostic accuracy for melanoma can be increased by up to 49% [13,14]. Histology is considered to be the gold standard for diagnosis. Additional stains including melan-A/MART-1 stain was found to aid in the detection of invasive disease in 29% of melanoma cases [15]. Histologically LM is characterized by atypical melanocytes proliferating along the dermo-epidermal junction as single cells or nests. Pagetoid spread may be minimal or absent. In contrast, LMM displays atypical melanocytes in single cells and nests within the dermis [16]. The diagnosis of LM and LMM can be challenging due to the extent of ultraviolet damage and/or prior therapeutic intervention like cryosurgery or topical treatments [11]. The dermoscopic features also vary with the site of the melanoma, histological type and depth of invasion (Table 1) [9].

**Objectives**

To review publications covering the dermoscopic features of pigmented macules on the head and neck.

**Methods**

Embase and PubMed (Medline) database from January 2015 to January 2021 were searched. A 4-step systematic review was conducted. The first step used keywords including dermoscopy/dermatoscopy or epiluminescence microscopy. In the second step studies covering melanoma, LM, LMM, LPLK, solar lentigo (SL), SK, pigmented actinic keratosis (PAK), pBD, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) were identified. Studies conducted on the head and neck were included in the third search step. The last step was combining the above three steps.

This review was structured according to the Preferred Reporting Items for Systematic Reviews and Metanalyses (PRISMA) guidelines. To identify all relevant studies the reference section of the studies was searched for studies not identified by the search. Where possible, some authors were contacted. Studies on raised lesions and those studies based exclusively on reflectance confocal microscopy (RCM) were excluded. Other exclusion criteria were studies based on surgical or medical treatments as well as studies based on conjunctiva and other mucosal surfaces. Finally, abstract only and non-English studies were also excluded.

| Dermoscopic Features                  | LMM            | LMM- in situ | P value |
|---------------------------------------|----------------|--------------|---------|
| Asymmetry                             | 24 (60%) (κ = 1) | 12 (60%) (κ = 0.65) | $P = 0.0001$ |
| Pseudo-network                        | 24 (60%) (κ = 0.80) | 8 (40%) (κ = 0.70) | $P = 0.0005$ |
| Irregular dots                        | 32 (80%) (κ = 0.83) | 15 (75%) (κ = 1) | $P = 0.121$ |
| Scar-like depigmentation              | 12 (30%) (κ = 0.86) | 6 (30%) (κ = 0.69) | $P = 0.032$ |
| 2 different colors                    | 32 (80%) (κ =1) | 15 (75%) (κ = 0.83) | $P = 0.005$ |
| 3 different colors                    | 8 (20%) (κ =1) | 5 (25%) (κ = 0.80) | $P = 0.005$ |
| 4 different colors                    | –              |              | $P = 0.0005$ |

**Table 1.** Cengiz et al 2015. Dermoscopic Features according to the histological subtype of melanoma on the head and neck.
Clinical and Dermoscopic Features of LM and LMM on the Head and Neck

The following extra-facial dermoscopy features: pseudo-pods, radial streaming, blue white veil, irregular blotches, scar-like depigmentation and atypical pigment network were recorded in low frequencies, (Table 2) [9]. In some studies the criteria of extra-facial LMM were found in only 52.4% of cases [17]. The typical clinical presentation is commonly a flat pigmented macule resembling other differentials including PAK/pBD/pIEC, LPLK, SL and SK [14,15].

The common reported dermoscopic features of facial melanoma were (Figure 1):

- Two or less colors and
- Asymmetric pigmented follicular openings (APFO) or folliculotropism,
- Brown colored globules and dots,
- Signet-ring like structures,
- A pattern of circles.
- Increased density of vascular network,
- Red rhomboid structures,
- Irregular dots (granularity or peppering),
- Atypical dots and globules (gray, slate gray or blue),
- Rhomboid gray/black structures,

In some studies multiple irregular gray/blue dots, referred to as “granularity” or “peppering”, were found in 93.5% of extra-facial melanoma, 26.5% of extra-facial benign lesions

| Dermoscopic Characteristics                              | N. (k= Kappa coefficient) | %   |
|----------------------------------------------------------|----------------------------|-----|
| Asymmetry in two axes                                    | 68 (k =1)                  | 63  |
| Atypical dots                                            | 80 (k =1)                  | 74.1|
| Radial streaming                                          | 32 (k =0.68)               | 29.6|
| Pseudopods                                               | 8 (k =0.92)                | 7.4 |
| Blue-white veil                                          | 20 (k =1)                  | 18.5|
| Mixed vascular pattern                                   | 44 (k = 0.92)              | 40.7|
| Scar-like depigmentation                                 | 64 (k = 0.87)              | 59.3|
| Rhomboidal Structures                                    | 32 (k = 0.85)              | 29.6|
| Atypical pigment network                                 | 26 (k = 0.92)              | 24  |
| Pseudo-network                                           | 32 (k = 0.84)              | 29.6|
| Asymmetric pigmented follicular openings                 | 56 (k =1)                  | 51.9|
| Annular-granular pattern                                 | 20 (k = 0.72)              | 18.5|
| Colors (3 or more)                                       | 40 (k = 0.88)              | 37  |
| Blotches                                                 | 8 (k = 1)                  | 7.4 |
| Increased density of vascular network                    | 35 (k = 0.95)              | 32.4|
| Red rhomboid structures                                  | 20 (k = 0.60)              | 18.5|
| Abrupt demarcation                                       | 11 (k = 0.76)              | 10  |
Accuracy of 0.72 for the diagnosis of LM seven criteria were found significant [21]. These criteria were:

- Asymmetric pigmented follicular openings,
- Rhomboid structures,
- Target-like pattern,
- Perifollicular gray color,
- Dark blotches,
- Moth eaten borders and
- Fingerprint-like structures.

In an attempt to differentiate between LM and PAK a “newly developed algorithm” claimed a diagnostic accuracy of 86.5%, sensitivity of diagnosis of LM versus PAK of 82.7%, specificity of 92.0%, positive predictive value (PPV) of 93.8% and negative predictive value (NPV) of 78.4%.

The eight statistically significant dermoscopic features for differentiation of LM from PAK were [4]:

- Light brown color,
- A structureless zone, varying in color from brown/tan to black,
- In focus discontinuous brown lines,
- Brown-to-gray incomplete circles,
- A brown or black structureless zone obscuring hair follicles,
- A brown (tan) eccentric structureless zone,
- A blue structureless zone and scales.

The features found to contribute the most to a diagnosis of LM were:

- Structureless zones ranging from brown/tan to black,
- Blue structureless zones,
- Brown to black structureless zones obscuring hair follicles and
- Incomplete brown to gray circles.

On the other hand the features suggestive of PAK were (Figure 4):

- The occurrence of light structureless zones,
- Brown (tan) eccentric scales and
- In focus brown discontinuous lines.

Clinical and dermoscopic features of PAK, pBD and pIEC

The main reported dermoscopic features of PAK, pBD and pIEC (Figure 4) were:

- Perifollicular erythema or red pseudo-network,
• White to yellow surface scale,
• Linear wavy vessels around hair follicles,
• Hair follicular openings surrounded by white halo,
• Evident follicles or follicular or keratotic plugs,
• Rosette sign (four dot clods, when polarized light dermoscopy is used) and
• Sharply demarcated borders.

In non-pigmented facial actinic keratosis (AK) four dermoscopic features were recorded [22], notably (Figure 4):

- Erythema surrounding the hair follicles or red pseudo-network (95%),
- White to yellow surface scale (85%),
- Linear wavy vessels around hair follicles (81%) and
- Hair follicle openings filled with yellow keratotic plugs (66%) and/or surrounded by white halo (100%).

These features collectively gave a picture of a “strawberry pattern”, (Figures 4 and 6).

Actinic keratoses tend to present as multiple macules on the same patient suggesting a “signature” pattern [22]. In lighter skin Fitzpatrick types these are usually non-pigmented AK while on darker skins they are pigmented [23]. Another clue to PAK on head and neck were “evident follicles” which were “visible follicles without pigmentation” and “projected as the dominant dermatoscopic feature” [2]. “Non-pigmented follicles associated with either interfollicular pigment, interfollicular erythema or both” was considered a strong dermoscopic clue to pIEC shared with PAK in the head and neck [24]. That description corresponded to the evident follicles described [2]. These dermoscopic findings were significantly positive for actinic keratosis in other studies [24], in addition to the rosette sign (also called four dot clods, seen with polarized light dermoscopy), large irregular linear vessels surrounding hair follicles and peripheral pigmentation [25]. Serpentine vessels were present in almost half of the cases of pIEC head and neck compared to coiled vessels in pIEC elsewhere [24]. A combination of red pseudo-network, hair follicular opening surrounded by a white halo and follicular plugs has been predicted to have a sensitivity of 90.7%, specificity of 81.82%, PPV of 90.70% and a NPV of 81.82% (Figure 6) [25].

For PAK/pBD scales show a PPV of 72.2% (specificity of 94.2%), white circles a PPV of 68.8% (specificity of 94.2%) and sharply demarcated borders a PPV of 44.2% (specificity of 86.0%), (Figure 6 and Table 3) [1]. The absence of scales in pigmented macules on the head and neck in combination with multiple colours with brown being present in all cases, as well pink, white and gray dominated in pigmented intraepidermal carcinoma (pIEC) in that location as per Inskip et al compared to Cameron et al [6,24]. In some studies, PAK/pBDs/pIEC had incomplete circles reported in 73.1% of cases compared to 71.3% for melanoma, nil reported circle in circle or double circles, nil reported gray structures, rhomboid structures in 94.7% compared to 91.7% in melanoma, nil dotted, serpentine or branched vessels, nil ulcerations and 86.0% well demarcated margins, (Table 3 and Figure 6) [1].

Figure 6. Macroscopy - Left side - A 43-year-old male with a pink, slightly scaly lesion located on the left temple. Dermoscopy - Right side - Dermoscopy features include a ‘strawberry’ appearance, with white-to-yellow follicular keratotic plugs (ellipse) surrounded by a whitish halo, and background erythema/red pseudo-network. In addition, 4-dot-structures (circles) are seen in some parts of the lesion, which when coalescing they form white complete circles (arrow). In parts of the lesion white lines are seen which are different from hairs (squares)-Fotofinder dermoscopy, Medicam 1000, magnification x20. Diagnosis: actinic keratosis.
Table 3. Tschandl et al 2015. Diagnostic indices of dermatoscopic clues to flat malignant facial lesions. Numbers in braces depict 95% confidence intervals.

|                      | RR (relative risk) | PPV (positive predictive value) | NPV (negative predictive value) | Sensitivity | Specificity |
|----------------------|--------------------|---------------------------------|---------------------------------|-------------|-------------|
| Melanoma             |                    |                                 |                                 |             |             |
| Any gray structure   | 8.9 (1.2–64.7)     | 13.3% (8.6–19.3)                | 98.5% (91.9–99.8)               | 95.8% (78.8–99.3) | 30.6% (24.5–37.2) |
| Vessels as dots      | 3.5 (1.1–11.8)     | 33.3% (5.3–77.3)                | 90.6% (86.1–94.0)               | 8.3% (1.3–27.0) | 98.1% (95.3–99.5) |
| Incomplete circles   | 3.0 (1.4–6.5)      | 18.4% (10.5–29.0)               | 93.9% (89.1–97.0)               | 58.3% (36.7–77.9) | 71.3% (64.8–77.2) |
| Gray circles         | 4.6 (2.2–9.7)      | 26.5% (15.0–41.1)               | 94.2% (89.9–97.1)               | 54.2% (32.8–74.4) | 83.3% (77.7–88.0) |
| Rhomboids            | 2.0 (0.7–5.3)      | 18.2% (5.3–40.3)                | 90.8% (86.2–94.3)               | 16.7% (4.8–37.4) | 91.7% (87.2–95.0) |
| Circle in a circle/double circle | 2.0 (0.3–12.3) | 20.0% (3.3–71.2)                | 90.2% (85.7–93.7)               | 4.2% (0.7–21.2) | 98.1% (95.3–99.5) |
| Basal cell carcinoma |                    |                                 |                                 |             |             |
| Any gray structure   | 7.7 (1.1–56.6)     | 11.6% (7.2–17.3)                | 98.5% (91.9–99.8)               | 95.2% (76.1–99.2) | 30.1% (24.1–36.7) |
| Branched vessels     | 17.8 10.5–30.3     | 100.0% (62.9–100.0)             | 94.4% (90.6–97.0)               | 38.1% (18.1–61.6) | 100.0% (98.3–100.0) |
| Serpentine vessels   | 12.2 (6.7–22.1)    | 83.3% (36.1–97.2)               | 93.2% (89.1–96.0)               | 23.8% (8.3–47.2) | 99.5% (97.5–99.9) |
| Ulceration           | 11.7 (6.0–22.7)    | 66.7% (33.0–89.9)               | 94.3% (90.5–96.9)               | 38.1% (18.2–61.6) | 98.2% (95.4–99.5) |
| Pigmented actinic keratosis/ Bowen disease | | | | | |
| White circles        | 3.0 (2.2–4.3)      | 68.8% (50.0–83.9)               | 77.4% (71.1–82.9)               | 31.9% (21.2–44.2) | 94.2% (89.5–97.2) |
| Sharply demarcated border | 1.7 (1.2–2.6) | 44.2% (29.1–60.1)               | 74.6% (68.0–80.5)               | 27.5% (17.5–39.6) | 86.0% (79.8–90.8) |
| Incomplete circles   | 1.7 (1.1–2.5)      | 39.5% (28.5–51.4)               | 76.2% (69.0–82.5)               | 43.5% (31.6–56.0) | 73.1% (65.8–79.6) |
| Rhomboids            | 2.3 (1.5–3.5)      | 59.1 (36.4–79.3)                | 74.3% (68.0–80.0)               | 18.8% (10.4–30.1) | 94.7% (90.2–97.6) |
| Four-dot clod        | 2.1 (1.0–4.5)      | 60.0% (15.4–93.5)               | 71.9% (65.7–77.6)               | 4.3% (1.0–12.2) | 98.8% (95.8–99.8) |
| Scale                | 3.4 (2.5–4.8)      | 72.2% (54.8–85.8)               | 78.9% (72.7–84.3)               | 37.7% (26.3–50.2) | 94.2% (89.5–97.2) |

Conclusions

The accurate diagnosis of LM and LMM is paramount for their early appropriate management. The differential diagnosis is variable. Different studies have compared different dermatoscopic features of LM, LMM, PAK, pBD and pIEC. Not all features were compared similarly. Some studies documented sensitivity and specificity while other publications listed the percentage of lesions showing the feature. Some compared positive predictive value (PPV) and negative predictive value (NPV) of the dermoscopy features. To date the used terminology is not unified in spite of some frequently used terms. Further studies are needed to agree on the criteria specific to each diagnosis, namely LM, LMM, PAK, pBD and pIEC. Furthermore, according to the current literature, there is a gap in the knowledge of site-specific dermatoscopic features on the head and neck. These site-specific areas include the ears, nose, cheeks, scalp and neck. The development of specific algorithms based on deep learning models (eg integrated scoring classifiers) could be of great help in differentiating LM/LMM of the head and neck from their simulators in clinical practice [26]. This would benefit from further studies.

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