



Difficult-to-diagnose facial melanomas: Utility of reflectance confocal microscopy in uncovering the diagnosis

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Melanoma on sun-damaged skin, commonly known as *lentigo maligna* (LM, akin to melanoma in situ) and *lentigo maligna melanoma* (akin to invasive melanoma), is mostly found on the head and neck of elderly patients. This type of melanoma, particularly when found early, may be difficult to diagnose on clinical inspection. Dermoscopy is a noninvasive imaging technique that aids in the identification of pigmented skin lesions and increases the diagnostic accuracy beyond naked eye examination.^{1,2} The dermoscopic criteria for facial LM were previously described. Because facial skin is characterized histopathologically by prominent adnexal openings, solar elastosis, and flattening of the dermoepidermal junction, the dermoscopic criteria of LM are distinct from those used for melanomas on the body and extremities.^{3,4} Moreover, the dermoscopic differentiation between facial LM and other nonmelanocytic diagnostic entities, such as pigmented actinic keratosis (pAK), solar lentigo, or lichen-planus–like keratosis can be challenging. In daily practice, when presented with a pigmented facial macule, the clinician must decide whether to biopsy the lesion and possibly leave a scar at a cosmetically sensitive site, follow up with the lesion, or treat it with nonsurgical modalities (eg, cryotherapy and topical creams). This decision may be hampered by some degree of diagnostic uncertainty. To aid in such a scenario, reflectance confocal microscopy (RCM) is a diagnostic device that uses a low-intensity laser light to produce high-resolution

Abbreviations used:

LM: Lentigo maligna
pAK: pigmented actinic keratosis
RCM: reflectance confocal microscopy

images of skin in vivo. A few of the key RCM features of LM are dendritic spindle-shaped cells extending down adnexal structures and nonedged papilla with pleomorphic nucleated cells at the dermoepidermal junction.⁵ When the clinical and dermoscopic diagnosis is equivocal, when lesions are poorly defined or lack pigmentation, or when the differential diagnosis is broad, RCM can aid in the diagnostic process of the solitary facial macule.

This report presents several cases of facial LM that are difficult to diagnose by clinical and dermoscopic features alone. We illustrate that in this diverse case series, features of melanoma were readily identified by RCM, and a straightforward diagnosis could be issued. Cases were selected to typify the presentations of small solitary macules or papules (cases 1 and 2) or mimickers of other diagnoses (cases 3 and 4).

METHODS

Illustrative RCM cases of histopathologically proven facial melanomas were selected from the image database collection of 2 skin cancer clinics in Italy and the United States. All images were captured using a commercially available RCM machine

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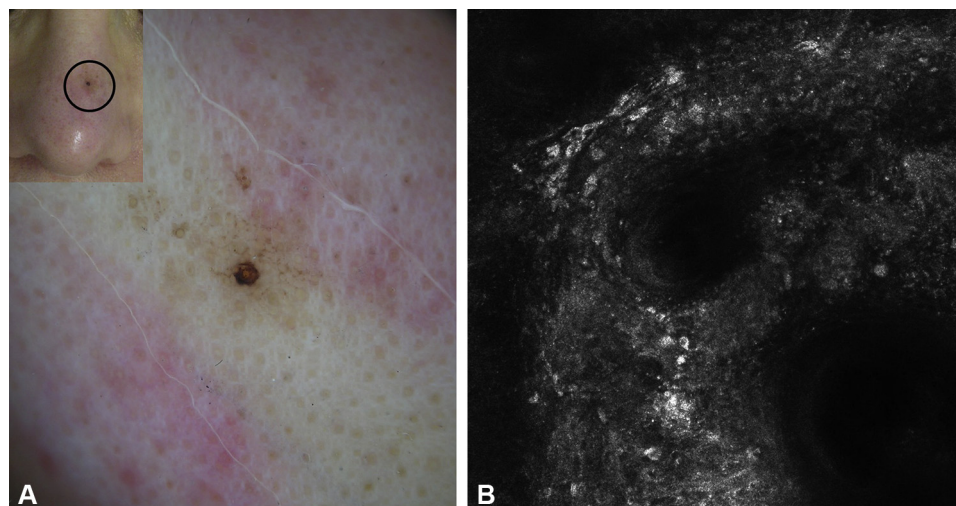


Fig 1. **A**, A small 2-mm macule on the dorsum of the nose with circumferential brown perifollicular pigmentation and grey circles. **B**, Reflectance confocal microscopy shows numerous bright pleomorphic cells surrounding the follicular opening at the suprabasilar epidermis.

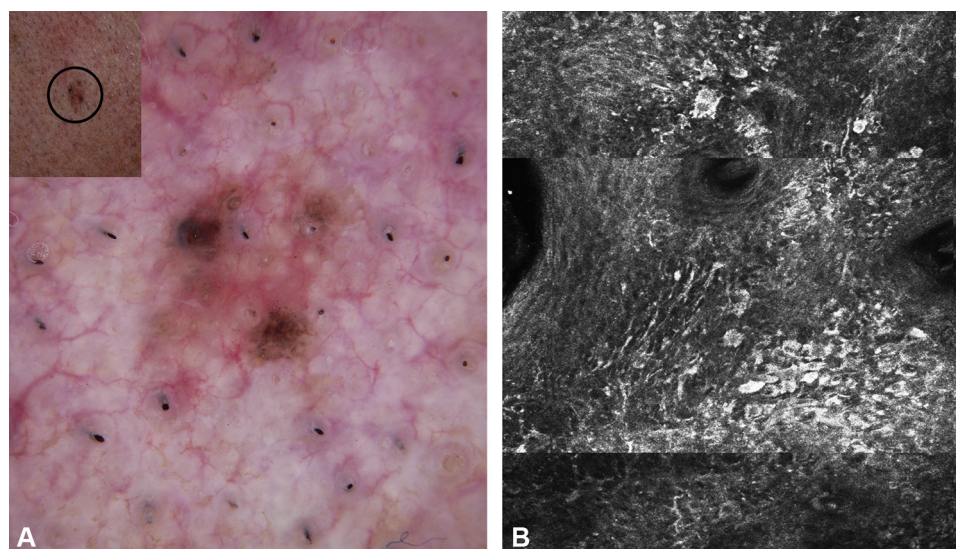


Fig 2. **A**, A 4-mm brown thin papule on the left cheek showed foci of gray dots and granules with perifollicular gray circles. **B**, Confocal microscopy examination showed sheets of pleomorphic roundish nucleated dendritic cells with descent along adnexal epithelium.

(Vivascope 1500, Caliber ID, Rochester, NY). Each case was analyzed by 2 experts on pigmented lesions and included only if there were no specific structures for melanoma, including criteria for LM, by clinical examination and dermoscopy.²

Case 1: Melanoma presenting as a small macule

A 60-year-old woman presented with a small 2-mm macule on the dorsum of the nose. By dermoscopy, there was circumferential brown perifollicular pigmentation surrounded by a tan structureless area and gray circles (Fig 1, A). The leading differential

diagnoses included solar lentigo, pigmented actinic keratosis, or seborrheic keratosis. However, RCM found numerous bright pleomorphic cells surrounding the follicular opening at the suprabasilar epidermis, suggestive of melanocytes in pagetoid spread, suggesting the diagnosis of melanoma (Fig 1, B). Subsequent histopathologic examination confirmed the diagnosis of melanoma in situ.

Case 2: Melanoma presenting as a small papule

A 60-year-old man presented with a 4-mm brown minimally palpable papule on his left cheek of unknown duration, incidentally noted during

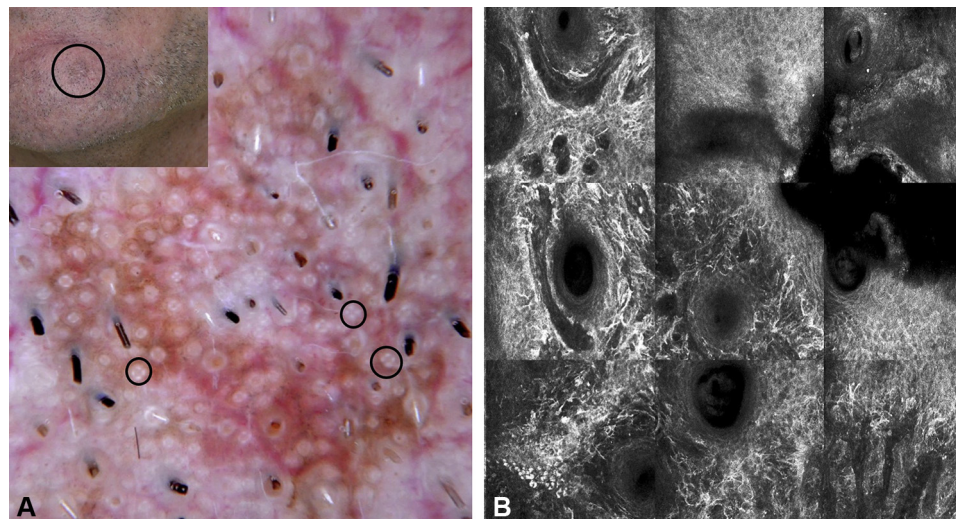


Fig 3. **A**, A tan-gray macule on the chin showed white circles filled with yellow-brown plugs and white shiny rosettes (circled) mimicking pigmented actinic keratosis or Bowen disease. **B**, Spindle-shaped bright cells surrounding the hair follicles are diagnostic for melanoma by confocal microscopy.

surgery for another skin lesion. Dermoscopic evaluation found 2 distinct foci of grey dots and granules and few peri-follicular gray circles (Fig 2, A). The differential diagnoses include melanoma on sun-damaged skin, lichen-planus–like keratosis or pAK. RCM examination found sheets of pleomorphic roundish nucleated and dendritic cells with descent along adnexal epithelium, features diagnostic for melanoma (Fig 2, B). The biopsy of the lesion found melanoma of 0.3 mm in Breslow thickness.

Case 3: Melanoma mimicking another diagnosis

A 54-year-old man with a history of facial LM noticed an enlarging tan-gray macule on the chin. Dermoscopic evaluation found white circles, keratotic plugs, and, by polarized light, white shiny structures arranged as rosettes (Fig 3, A). The leading diagnosis was a keratinocytic neoplasm, such as pAK or Bowen's disease. However, on RCM, there were spindle-shaped bright cells surrounding the hair follicles, features diagnostic for melanoma (Fig 3, B). Histopathologic examination confirmed melanoma in situ.

Case 4: Melanoma mimicking another diagnosis

A 75-year-old man presented with a brown patch on the cheek. Dermoscopic features present in this lesion included fingerprinting (brown parallel ridges and lines) and some gray circles (Fig 4, A). The leading diagnosis was solar lentigo. However, because this was a solitary lesion and gray circles

were noted, RCM examination was performed to confirm the dermoscopic diagnosis. In the upper epidermis, there was a proliferation of dendritic and numerous bright roundish cells as solitary units and as cordlike aggregates; these findings suggested the diagnosis of LM (Fig 4, B). In addition, there were foci with prominent bulbous epithelial projections consistent with a solar lentigo. Biopsy of the lesion found a collision lesion of melanoma in situ and adjacent solar lentigo (Fig 4, C and D).

DISCUSSION

In the case of a small brown macule or papule on the face, the clinician may be confronted with a broad differential diagnosis. By clinical examination, small-diameter LM are typically solitary, isolated lesions with fewer surrounding freckles and lack distinguishing dermoscopic criteria.⁶ To complicate matters, the classic dermoscopic criteria of LM, such as brown pseudonetwork and annular granular pattern, can also be seen in benign lesions such as pAK and lichen-planus–like keratosis.⁷ One clue may be the dermoscopic gray color in early and small-diameter facial lesions, which has been reported to be a sensitive sign for LM.⁸ Tschandl et al⁹ examined the dermoscopic features of 240 flat pigmented facial lesions from patients seen prospectively over a 5-year period. Their sample of LMs, which included small-diameter and thin neoplasms, lacked the classical dermoscopic criteria of rhomboids or circle within a circle, but the presence of gray structures was a clue to a malignant diagnosis, including LM, basal cell carcinomas, and pAK. Because RCM images a lesion

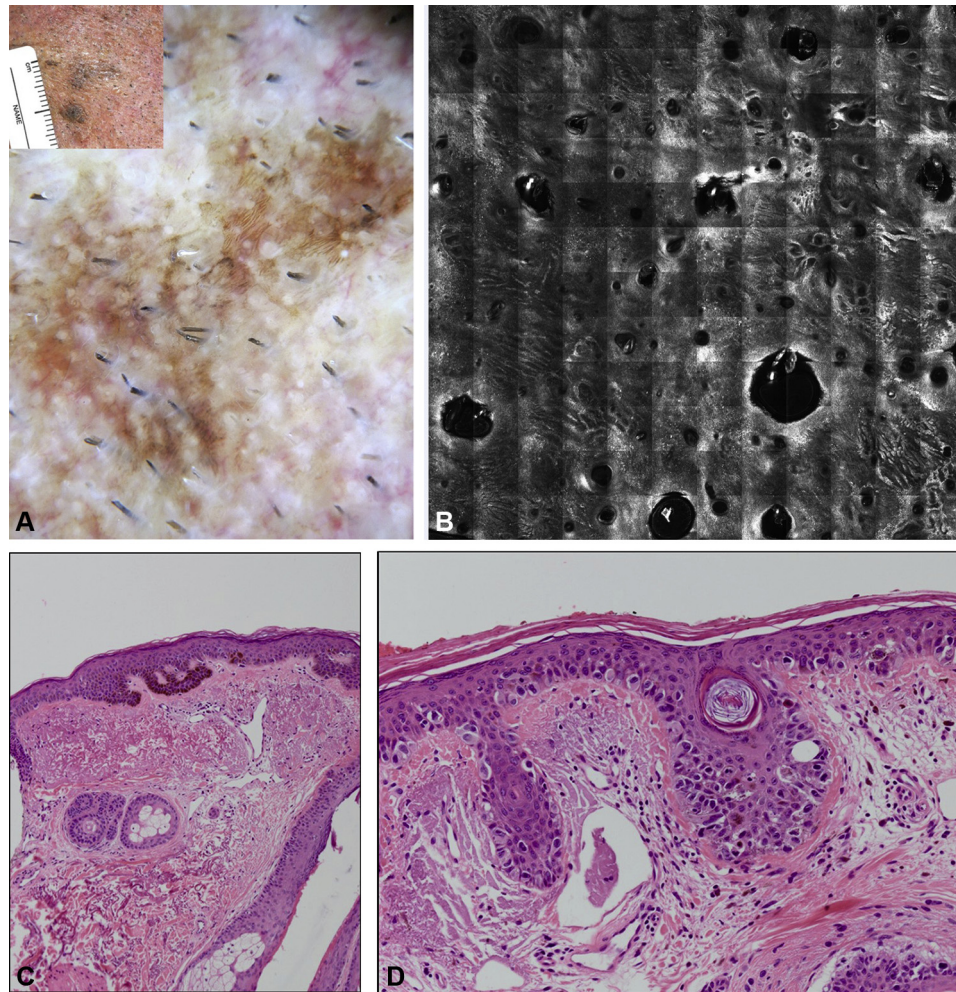


Fig 4. **A**, A large brown patch on the cheek contained dermoscopic features for solar lentigo (fingerprinting and gray circles). **B**, By confocal microscopy, there was a proliferation of dendritic and numerous bright roundish cells as well as tubular structures with prominent bulbous projections. Presence of these features was suspicious for a collision lesion, and histology confirmed the presence of solar lentigo (**C**) and melanoma in situ (**D**).

at a cellular-level resolution, the finding of a proliferation of melanocytes allows the exclusion of all nonmelanocytic entities from the differential diagnosis and the correct recognition of LM. As seen in our cases of small-diameter LMs with equivocal dermoscopic features, RCM clearly found a florid proliferation of atypical melanocytes.

Differentiating LM from its common mimickers is dermoscopically challenging, especially in cases showing criteria that are typically associated with other diagnostic entities, such as pAK or solar lentigo.¹⁰ Studies to examine the dermoscopic criteria for these pigmented facial lesions aimed to improve the diagnostic accuracy for detecting LM. Lallas et al¹¹ asserted that the presence of gray rhomboidal structures and absence of evident follicles favor the diagnosis of LM, whereas a scaly surface and white

circles favor pAK. In contrast, Akay et al¹² reported striking similarities between dermoscopic features of LM and its mimickers, especially those features that are classically associated with LM such as annular-granular structure, asymmetrical pigmented follicular openings, and black globules.¹² The patient in case 3 had rosette structures, which are most commonly associated with keratinocytic neoplasms, such as squamous cell carcinomas and actinic keratosis.¹³ These can be visible under polarized light as 4 shiny white dots arranged as a 4-leaf clover. The etiology is likely alternating focal hyperkeratosis and horn-filled adnexal openings.¹⁴ The presence of rosettes, in the context of scale and red color are more suggestive of an actinic keratosis. Rosettes have only been reported in a handful of cases of melanoma.^{9,14,15} Again, RCM clearly found features

diagnostic for melanoma. Fingerprinting, as demonstrated in case 4, is a dermoscopic feature mainly seen in benign lesions such as solar lentigo and seborrheic keratosis; however, in this case, RCM found a concurrent LM. Indeed, among collision tumors between melanoma and a benign entity, seborrheic keratosis is the most common benign counterpart.¹⁶ Although the melanoma component in a collision lesion may not always be recognizable by dermoscopy, RCM provides great benefit in the correct identification of the melanoma.¹⁷

RCM, when combined with dermoscopy, can increase the diagnostic accuracy for melanoma.^{5,18} Compared with the current gold standard, RCM can achieve concordance with histopathology in 89% of cases.¹⁹ It is in our experience that most melanomas on sun-damaged facial skin are isolated lesions. Our difficult-to-diagnose cases showed few melanocytic-specific dermoscopic features; however, these cases had an unequivocal RCM diagnosis of melanoma. Despite their feature-poor dermoscopic presentation, the cases presented here showed clear-cut diagnostic RCM features such as florid proliferation of atypical melanocytes, pagetoid spread, and cellular pleomorphism. We showed the applicability of RCM in the clinical setting for difficult-to-diagnose facial melanomas presenting as small lesions and as mimics of benign nonmelanocytic neoplasms.

REFERENCES

1. Kittler H, Pehamberger H, Wolff K, Binder M. Diagnostic accuracy of dermoscopy. *Lancet Oncol*. 2002;3:159-165.
2. Argenziano G, Soyer HP. Dermoscopy of pigmented skin lesions—a valuable tool for early diagnosis of melanoma. *Lancet Oncol*. 2001;2:443-449.
3. Stolz W, Schiffrer R, Burgdorf WH. Dermoscopy for facial pigmented skin lesions. *Clin Dermatol*. 2002;20:276-278.
4. Cengiz FP, Cengiz AB, Emiroglu N, Comert E, Wellenhof RH. Dermoscopic and clinical features of head and neck melanoma. *An Bras Dermatol*. 2015;90:488-493.
5. Guitera P, Pellacani G, Crotty KA, et al. The impact of in vivo reflectance confocal microscopy on the diagnostic accuracy of lentigo maligna and equivocal pigmented and nonpigmented macules of the face. *J Invest Dermatol*. 2010;130:2080-2091.
6. Todorovic-Zivkovic D, Argenziano G, Lallas A, et al. Age, gender, and topography influence the clinical and dermoscopic appearance of lentigo maligna. *J Am Acad Dermatol*. 2015;72:801-808.
7. Sahin MT, Ozturkcan S, Ermertcan AT, Gunes AT. A comparison of dermoscopic features among lentigo senilis/initial seborrheic keratosis, seborrheic keratosis, lentigo maligna and lentigo maligna melanoma on the face. *J Dermatol*. 2004;31:884-889.
8. Todorovic-Zivkovic D, Zalaudek I, Lallas A, Stratigos AJ, Piana S, Argenziano G. The importance of gray color as a dermoscopic clue in facial pigmented lesion evaluation: a case report. *Dermatol Pract Concept*. 2013;3:37-39.
9. Tschandl P, Rosendahl C, Kittler H. Dermoscopy of flat pigmented facial lesions. *J Eur Acad Dermatol Venereol*. 2015;29:120-127.
10. de Carvalho N, Farnetani F, Ciardo S, et al. Reflectance confocal microscopy correlates of dermoscopic patterns of facial lesions help to discriminate lentigo maligna from pigmented nonmelanocytic macules. *Br J Dermatol*. 2015;173:128-133.
11. Lallas A, Tschandl P, Kyrgidis A, et al. Dermoscopic clues to differentiate facial lentigo maligna from pigmented actinic keratosis. *Br J Dermatol*. 2016;174:1079-1085.
12. Akay BN, Kocuyigit P, Heper AO, Erdem C. Dermoscopy of flat pigmented facial lesions: diagnostic challenge between pigmented actinic keratosis and lentigo maligna. *Br J Dermatol*. 2010;163:1212-1217.
13. Liebman TN, Rabinovitz HS, Dusza SW, Marghoob AA. White shiny structures: dermoscopic features revealed under polarized light. *J Eur Acad Dermatol Venereol*. 2012;26:1493-1497.
14. Gonzalez-Alvarez T, Armengot-Carbo M, Barreiro A, et al. Dermoscopic rosettes as a clue for pigmented incipient melanoma. *Dermatology*. 2014;228:31-33.
15. Liebman TN, Scope A, Rabinovitz H, Braun RP, Marghoob AA. Rosettes may be observed in a range of conditions. *Arch Dermatol*. 2011;147:1468.
16. Cascajo CD, Reichel M, Sanchez JL. Malignant neoplasms associated with seborrheic keratoses. An analysis of 54 cases. *Am J Dermatopathol*. 1996;18:278-282.
17. Moscarella E, Rabinovitz H, Oliviero MC, et al. The role of reflectance confocal microscopy as an aid in the diagnosis of collision tumors. *Dermatology*. 2013;227:109-117.
18. Ferrari B, Pupelli G, Farnetani F, et al. Dermoscopic difficult lesions: an objective evaluation of reflectance confocal microscopy impact for accurate diagnosis. *J Eur Acad Dermatol Venereol*. 2015;29:1135-1140.
19. Menge TD, Hibler BP, Cordova MA, Nehal KS, Rossi AM. Concordance of handheld reflectance confocal microscopy (RCM) with histopathology in the diagnosis of lentigo maligna (LM): a prospective study. *J Am Acad Dermatol*. 2016;74:1114-1120.