A pigmented macule on the nose
What is your diagnosis?

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The differential diagnosis of pigmented macules of the face can be challenging. Dermoscopy may help, and adding confocal microscopy improves sensitivity and specificity; histopathology, however, remains the gold standard.

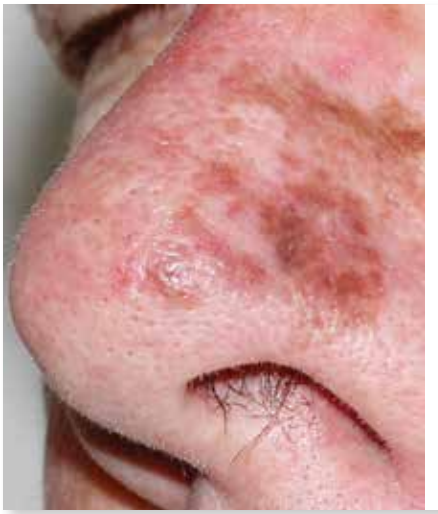

Figure 1. Lentigo maligna. The irregular pigmented macule of two colours on the left side of the patient's nose.

CASE PRESENTATION

A man in his 60s presented for a full skin check. He had heavily sun-damaged skin and a past history of lentigo maligna on the nose that was treated three years ago with cryotherapy and imiquimod. He had noted some new pigmentation arising in that area. On clinical examination, an irregular pigmented macule of two colours was seen (Figure 1). Differential diagnoses included solar lentigo, flat seborrhoeic keratosis, pigmented actinic keratosis and, most importantly, recurrent lentigo maligna.

Dermoscopic examination showed homogeneous light brown pigmentation, asymmetrical hyperpigmented follicular openings, granular blue-grey pigmentation and rhomboidal structures (Figures 2a to c). As the borders of the lesion were very uneven, an in vivo reflectance confocal microscope (RCM) was used to confirm the diagnosis and map the area to treat (Box). The RCM image of the epidermis showed multiple atypical large bright round cells (Figure 3), a characteristic feature for pagetoid spread. (Pagetoid cells are cells, melanocytes in this case, that invade the upper epidermis from below. In RCM, they are seen as large bright round cells or as pleomorphic cells with dendritic processes.) A biopsy was performed and the pathology report

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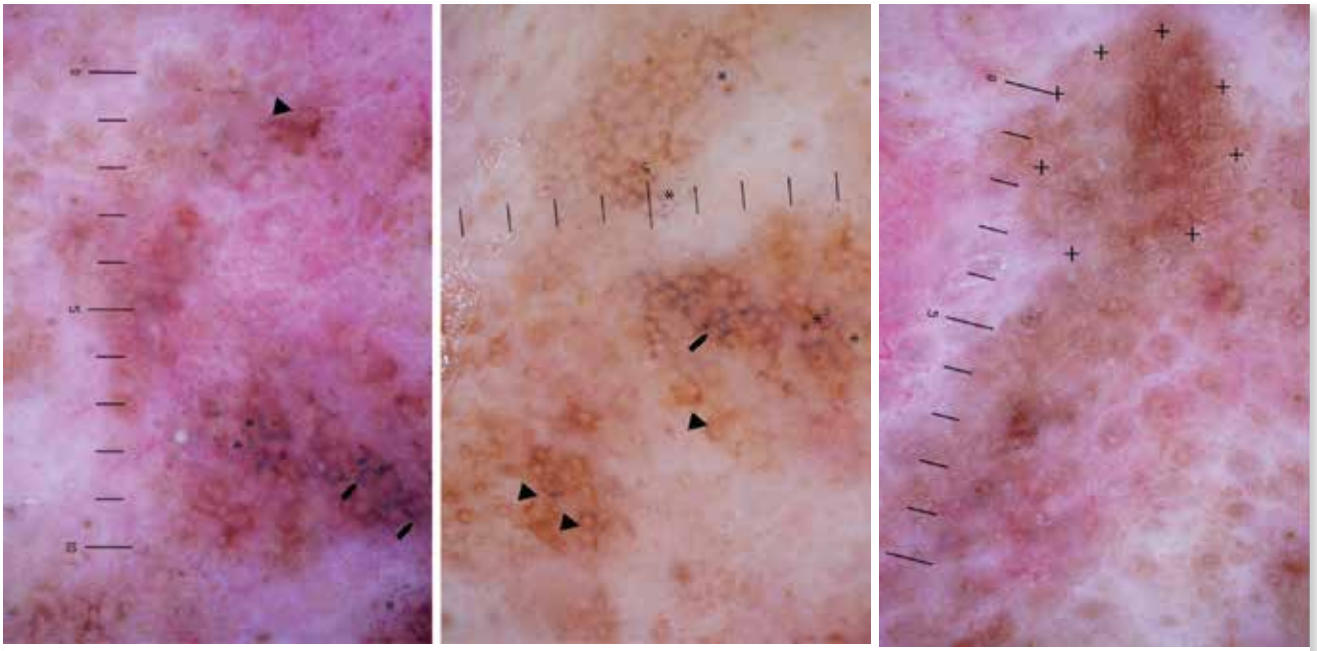

Figures 2a to c. Dermoscopic examination of the lentigo maligna in Figure 1. a and b (left and centre). Asymmetrical hyperpigmented follicular openings (triangles), granular blue-grey pigmentation (asterisks) and rhomboidal structures (arrows). c (right). Homogeneous light brown pigmentation (plus signs).

confirmed the diagnosis of lentigo maligna, ruling out a dermal component.

DISCUSSION

Lentigo maligna is the most frequent type of melanoma on the face. Most authors refer to the entity as 'lentigo maligna' when it is confined to the epidermis (in situ) and as 'lentigo maligna melanoma' when it invades the dermis.[1]

REFLECTANCE CONFOCAL MICROSCOPY

Reflectance confocal microscopy (RCM) allows 'optical' biopsy of the epidermis and superficial dermis (to a maximum of 0.2 mm deep). Compared with dermoscopy, which allows the observation of patterns and features of skin lesions, RCM provides a much sharper image and allows assessment of tissue underlying dermoscopic features at a cellular level, also in the horizontal plane.

Melanin provides a strong contrast in the black and white images of RCM as it backscatters the laser beam, making pigmented cells appear bright. RCM is therefore useful in the assessment of pigmented skin lesions, enabling the size, shape and organisation of the pigmented cells to be readily assessed. RCM is also of use in the evaluation of skin lesions that are not pigmented.

Lentigo maligna tends to occur in chronically sun-exposed areas, mostly on the face and neck. Its incidence is increasing, and has a peak between the ages of 60 and 80 years.

It can be difficult to make the differential diagnosis of pigmented macules of the face with the naked eye, as non-melanocytic lesions and melanocytic lesions have the same appearance. Dermoscopy helps to make the diagnosis; however, classic melanoma dermoscopy criteria cannot be applied to pigmented lesions on the face. Dermoscopic characteristics of lentigo maligna and lentigo maligna melanoma are summarised in the Table.[1,2]

A progression growth model for lentigo maligna has been described (Figure 4).[3] In the early phase, hyperpigmented asymmetrical follicular openings can be observed, then fine dots and globules appear, forming the annular–granular pattern. When the lentigo maligna becomes invasive, pigmented rhomboidal structures appear and then, as the hyperpigmentation coalesces, follicular openings become obliterated. These features, however, are not all specific for melanoma, as several lesions can simulate the early changes seen in lentigo maligna.

Lentigo maligna/lentigo maligna melanoma should be distinguished from the differential diagnoses of melanocytic naevus, flat seborrhoeic keratosis (lentigo senilis), lichen planus-like keratosis and pigmented actinic keratosis. Flat seborrhoeic keratosis usually shows horn pseudocysts, yellow

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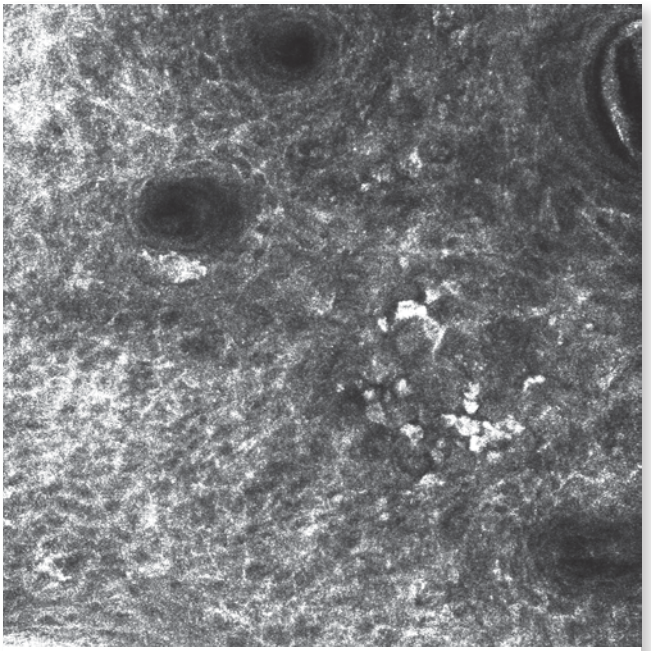

Figure 3. Reflectance confocal microscopy of the lentigo maligna in Figure 1, showing epidermis with multiple atypical large bright pagetoid cells (round and dendritic). (Image 5 µm x 5 µm.)

opaque areas, milia-like cysts, fingerprint-like structures, moth-eaten borders and the jelly sign; the lesions may, however, simulate streaks, and thicker lesions can show blue-grey areas and pseudofollicular openings.[4] Lichen planus-like keratosis, a form of irritated seborrhoeic keratosis, may have grey dots and globules. Pigmented actinic keratosis also may have grey dots and annular–granular structures but can be differentiated from lentigo maligna/lentigo maligna melanoma by their rough surface, their tendency to be grouped and the usual lack of asymmetrical pigmented follicular openings.[5,6]

The most specific finding that can help differentiate lentigo maligna/lentigo maligna melanoma from other lesions is the presence of asymmetrical hyperpigmented follicular openings.[2] The finding of one or more of the features of lentigo maligna in a melanocytic macule of the face suggests the lesion may be malignant, and a biopsy or at least long-term (six months) digital monitoring should be considered.[7]

Good clinicopathology correlation is necessary as a small sample of a large lesion may not be indicative of the final diagnosis. Large shave biopsy is the preferred mode of diagnosis. If the lesion is growing, a further biopsy specimen should be obtained. Of note, it is very rare to have a new dysplastic naevus on the face of a patient older than 60 years, and the clinician should review the diagnosis with the pathologist in case of discrepancy.

In vivo confocal microscopy features for lentigo maligna

TABLE. DERMOSCOPIC CHARACTERISTICS OF LENTIGO MALIGNA AND LENTIGO MALIGNA MELANOMA[1,2]

Criteria	Description
Classic Stolz criteria (ordered by progression)[2]	
Asymmetrical hyperpigmented follicular opening*	Pigment around the follicular openings, often irregularly distributed Histologically corresponds to lentigo maligna invasion of hair shaft
Annular–granular pattern	Fine grey dots and globules around the follicles Mainly caused by melanin and macrophages, not by melanoma cells
Pigmented rhomboidal structures*	Pigment around the follicular openings is more dense, forming a rhomboidal shape Associated with invasion
Obliterated hair follicles	Pigmentation coalesces and obliterates the follicular openings Associated with invasion
New criteria proposed by Pralong[1]	
Darkening on dermoscopic examination	The lesion appears darker when observed with dermoscopy compared with the naked eye
Target-like pattern	Dark dot in the centre of the dark circle of a hyperpigmented hair follicle
Increased density of the vascular network	Vascular network of higher density within the lesion
Red rhomboidal structures	Vessels distributed around the hair follicles in rhomboidal shape Associated with invasion
Other criteria	
Regression-associated features	Peppering – grouping of fine grey dots and globules White scar-like areas (advanced melanoma)
Vertical growth-associated features	Ulceration Black structureless areas Blue papular areas
Classic features of extrafacial melanoma	Multiple colours, atypical honeycomb-like pigment network, irregularly distributed globules, dots and streaks

* Asymmetrical hyperpigmented follicular openings and pigmented rhomboidal structures are the most specific features for lentigo maligna and lentigo maligna melanoma.

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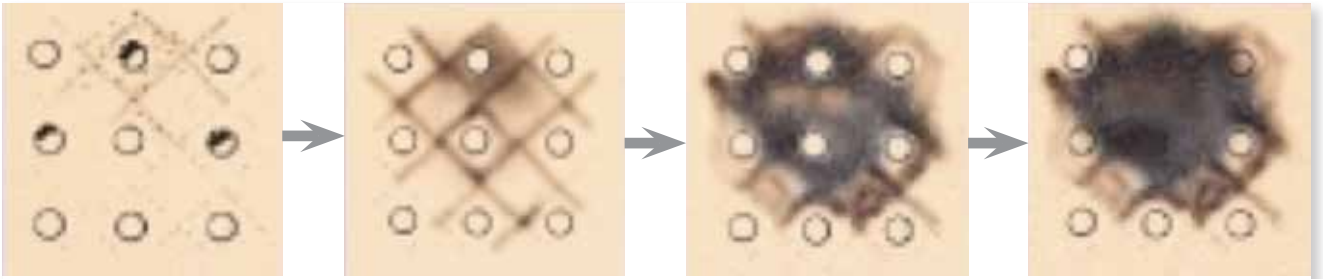

Figure 4. Progression growth model for lentigo maligna described by Schiffner.[3] From left to right: hyperpigmented asymmetrical follicular openings; fine dots and globules (annular–granular pattern); pigmented rhomboidal structures; hyperpigmentation coalesces and follicular openings become obliterated.

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and lentigo maligna melanoma have been described, and this technique has been proposed to add sensitivity and specificity to the diagnosis made on dermoscopy, to help target biopsy at the worst area and to map extensive or recurrent lesions, particularly in cosmetically challenging cases.[8-12]

The first line of management for lentigo maligna is complete excision with at least 5 mm margins, which is sometimes difficult to achieve. Second-line treatments are radiotherapy and imiquimod, and these should be discussed in a specialist environment.

CONCLUSIONS

Dermoscopy has demonstrated its utility in assessing pigmented lesions on the face. These lesions, however, do not show the classic melanoma criteria seen elsewhere on the body and the sensitivity of lentigo maligna criteria is not very high. In vivo confocal microscopy has been proposed for difficult cases, although this technology is only available in a few specialised institutions in Australia. Patients in whom diagnosis or management are challenging should be referred to these centres.

KEY POINTS

- The differential diagnosis of pigmented macules on the face can be challenging.
- Dermoscopy may help with the diagnosis, but it is still far from an exact science as some benign lesions have similar features to lentigo maligna.
- Confocal microscopy combined with dermoscopy adds sensitivity and specificity to the diagnosis.
- Histopathology remains the gold standard for diagnosis. MT

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