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BRIEF REPORTS

Unstable solar lentigo: A defined separate entity

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ABSTRACT

An unstable solar lentigo is a solar lentigo with areas of melanocytic hyperplasia not extending past the margin of the lesion. They are discrete, macular, pigmented lesions arising on sun-damaged skin and a subset of typical solar lentigos. Clinically they differ from usual solar lentigines in often being solitary or larger and darker than adjacent solar lentigines. These lesions are of clinical importance as they can arise in close proximity to lentigo maligna and in a single lesion there can be demonstrated changes of solar lentigo, unstable solar lentigo and lentigo maligna. These observations led us to conjecture that unstable solar lentigos could be a precursor lesion to lentigo maligna. In this article we examine the possibility that lentigo maligna can arise within a solar lentigo through an intermediate lesion, the unstable solar lentigo. We propose that the histopathological recognition of this entity will allow for future research into its behaviour and thus management. We review difficulties in the diagnosis of single cell predominant melanocytic proliferations and the concept of unstable lentigo in view of the literature and clinical experience supporting the proposal of its recognition as a separate entity.

Key words: lentigo maligna, melanoma, precursor lesion, solar lentigo, unstable lentigo.

INTRODUCTION

Skin cancer is a significant malignancy in Australia, which has the world's highest annual incidence rate of melanoma and keratinocyte cancers (basal cell carcinomas and squamous cell carcinomas).[1,2] The main environmental risk factor for the development of skin cancer is UV radiation. Accompanying this are the other cutaneous changes of chronic solar damage such as elastosis, solar keratosis and solar lentigines. An unstable solar lentigo is a solar lentigo that shows increased numbers of melanocytes which may be larger than usual but lack nuclear atypia or hyperchromasia.[3] There is no pagetoid spread, nesting of melanocytes or extension of melanocytes down adnexal structures. Melanocytic proliferation does not extend beyond the margin of the solar lentigo into the surrounding skin. In this article we review the concept of the unstable solar lentigo in the light of current and past work.

CLINICAL CHARACTERISTICS

The solar lentigo presents as an irregular brown or tan macule on areas of sun-exposed skin such as the face and the back of the hands.[3,4] They typically occur in elderly, fair-skinned people who have had excessive exposure to the sun. Under the dermatoscope, the solar lentigo can display diffuse brown pigmentation, light-brown fingerprint-like structures and a fine regular network. The surface may be rough on palpation and dermoscopically there may be comedo-like openings, as these lesions are often in the process of evolving into seborrhoeic keratoses.[5]

The unstable solar lentigo typically presents as an isolated, irregularly pigmented macule on a background of solar damage (Fig. 1). They often stand out as being solitary lesions or markedly different to surrounding solar lentigines. They are typically larger in size, darker in colour and more irregular. Background erythema and areas of regression may be present. Dermoscopic findings may include perifollicular pigment asymmetry, a varied network or pseudo-network, blue-grey areas and variable pigmentation. During clinical follow up these lesions darken and enlarge, and the edges sometimes become more distinctive. We have observed lesions with clinical,

Abbreviations:

LM	lentigo maligna *in situ*
LMM	lentigo maligna melanoma
XP	xeroderma pigmentosum

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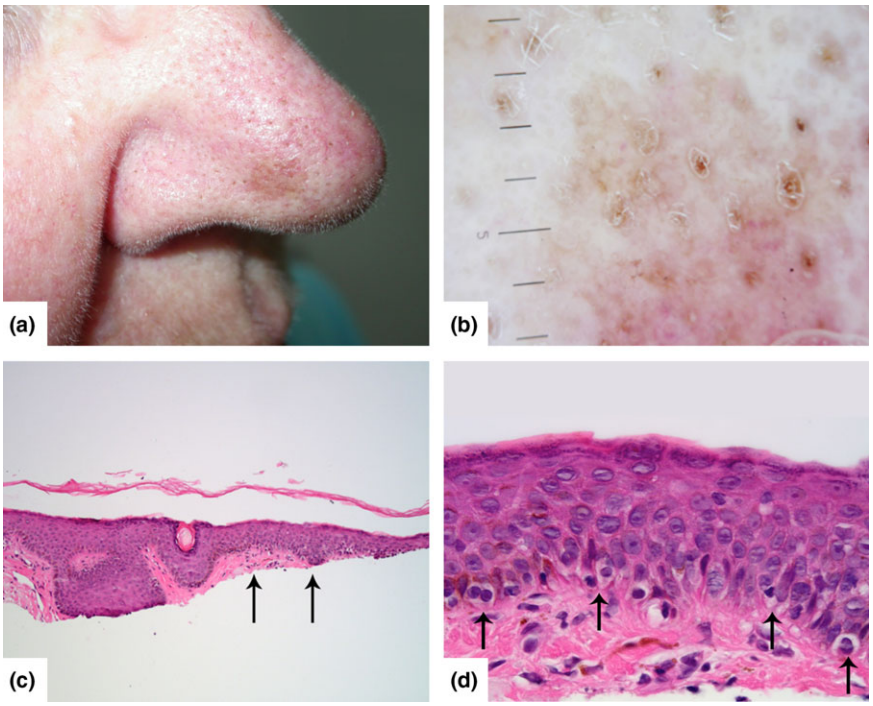

Figure 1 (a) An unstable solar lentigo. An isolated centro-facial lentigo-like lesion. (b) Dermoscopy of unstable solar lentigo demonstrating pseudo-network, background erythema and subtle perifollicular pigment asymmetry. (c) Shave biopsy of unstable solar lentigo demonstrating basilar hyperpigmentation and increased number of normal melanocytes (arrows). (d) Histology of unstable solar lentigo demonstrating increased number of normal melanocytes (arrows).

dermoscopic and histopathological features of solar lentigo, unstable solar lentigo and lentigo maligna within the one lesion.

Lentigo maligna also presents as an irregularly pigmented dark brown to black macule, usually darker in colour than a solar lentigo.[3,4,6] They occur on sun-exposed areas of elderly patients, in particular the upper cheek, temple, or forehead. They can also occur on other sun-exposed sites such as the legs, arms and back of the hands. Lentigo maligna can develop into invasive melanoma but the evolution to invasive disease is typically very slow. Not infrequently, the invasive melanomas that develop in lentigo maligna are of the desmoplastic or spindle cell type.[7] Dermoscopy of lentigo maligna demonstrates characteristic features, including atypical pseudo-networks, asymmetrical pigmented follicular openings, rhomboidal structures, annular or granular structures and a grey pseudo-network.[5]

HISTOLOGICAL CHARACTERISTICS

A classic solar lentigo is a lesion composed of keratinocytes. The keratinocytes subtly enlarge and proliferate, creating elongation of the rete ridges and thickening of the epidermis. The number of melanocytes may be mildly increased along the dermal-epidermal junction but melanocytic hyperactivity is characteristic and is reflected by the hyperpigmentation of the basal keratinocytes. There is solar elastosis in the dermis (Fig. 2).

An unstable solar lentigo is both a proliferation of keratinocytes and melanocytes. Within a background of classic solar lentigo, melanocytes proliferate as single cells at the level of the basal layer (Figs 1,2). Naevo-melanocytes are not observed. The single melanocytes do not proliferate side by side but each is separated by a few keratinocytes. No upward migration of melanocytes is seen and deep extension down adnexal structures is not seen. The melanocytes are not atypical and have round nuclei. The sickle shaped nuclei and partial upward migration of reactive melanocytic hyperplasia are not seen. The melanocytic hyperplasia ceases at the edges of the solar lentigo. Beyond the solar lentigo, melanocytic hyperplasia is not observed.

Lentigo maligna is a melanocytic lesion without a keratinocytic component. Atypical melanocytes proliferate largely as single cells at the basal layer of the epidermis; there are poorly formed, randomly distributed melanocytic nests along the dermal-epidermal junction. The melanocytes also extend into adnexal structures such as hair follicles and eccrine ducts. The epidermis is variably atrophied and the upper dermis demonstrates marked solar elastosis. Lentigo maligna does not generally have distinct margins.

DISCUSSION

Solar lentigines are keratinocytic lesions, which develop on a background of chronic sun damage. Aoki and colleagues[8] have suggested that the mutagenic effects of

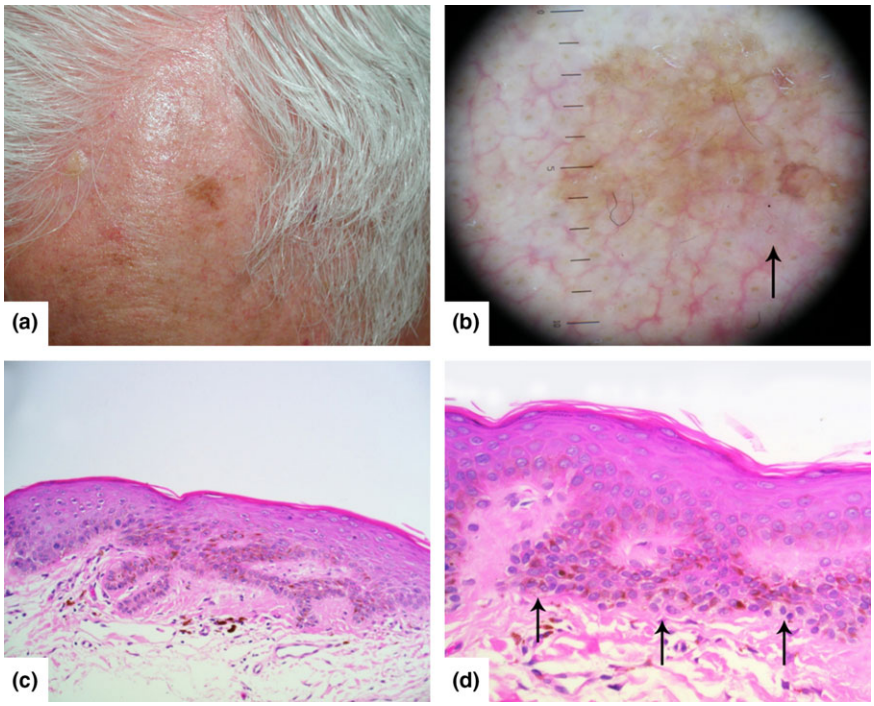

Figure 2 (a) A large, isolated lentigo-like lesion demonstrating changes consistent with an unstable solar lentigo and solar lentigo within the same lesion. (b) Dermoscopy of an unstable solar lentigo and solar lentigo within the same lesion, demonstrating subtle perifollicular pigment asymmetry, blue-grey areas, pseudo-network and variable pigmentation. Note the incidental basal cell carcinoma with typical arborising vessel (arrow). (c) Unstable solar lentigo and solar lentigo within the same lesion. Histology of solar lentigo demonstrating enlarged keratinocytes and thickening of the epidermis. (d) Unstable solar lentigo and solar lentigo within the same lesion. Histology of unstable solar lentigo demonstrating increased number of normal melanocytes (arrows).

previous repeated UV exposure induce the development of solar lentigines. The upregulation of genes related to melanin production is more prominent than melanocyte proliferation, supporting the notion that solar lentigo is typically a proliferation of keratinocytes containing normal numbers of hyperactive melanocytes.

An unstable solar lentigo is a solar lentigo with melanocytic hyperplasia not extending past the margin of the lesion. Clinically these lesions are isolated, often centrofacial and larger than other facial solar lentigines. Additionally they can represent histological characteristics on a continuum between a solar lentigo and lentigo maligna. Reactive melanocytic hyperplasia may mimic unstable solar lentigo. Reactive melanocytic hyperplasia tends to be composed of small, sickle shaped melanocytes that extend partially upward into higher levels of the epidermis. In contrast to unstable solar lentigo, a reactive melanocytic hyperplasia will not respect the boundary of the solar lentigo and will not produce significant basal pigmentation.

The widespread atypical melanocytosis found in chronically sun-exposed skin poses a challenge to dermatopathologists attempting to assign a specific name to a melanocytic proliferation. This issue is a particular diagnostic problem in regions with high solar irradiation. Atypical melanocytic hyperplasia is a term used to define basilar single cell melanocytic proliferations with no significant circumscription or melanocytic nesting that falls short of criteria for lentigo maligna. Atypical melanocytic hyperplasia can occur in chronically sun-damaged skin in the absence of a clinically apparent lesion. This may be over-interpreted histopathologically in this context as a true melanocytic lesion. Hendi and colleagues analysed chronically sun-damaged non-lesional skin in 100 patients and found areas with high melanocyte density, a mild to moderate confluence of melanocytes, focal upward migration of melanocytes, superficial follicular extension and mild to moderate cytological atypia; all features of lentigo maligna. This atypical melanocytic hyperplasia found in chronically sun-damaged skin may run through a coincident solar lentigo; however, as this finding does not respect the boundary of the lesion, it should not be categorised as unstable solar lentigo. [9]

Being a feature of chronically sun-damaged skin atypical melanocytic hyperplasia is often adjacent to lentigo maligna, creating difficulties in the histopathological assessment of the excision margin.[10] The distinguishing criteria for the diagnosis of melanoma *in situ* compared to melanocytic hyperplasia have been identified as the presence of nests of melanocytes, the irregular distribution of melanocytes, the descent of melanocytes down adnexal epithelial structures, the irregular distribution of pigment, the presence of melanocytes above the junction, a high number of melanocytes, pleomorphism of melanocytes and atypical nuclei of melanocytes.[11] As the margins of lentigo

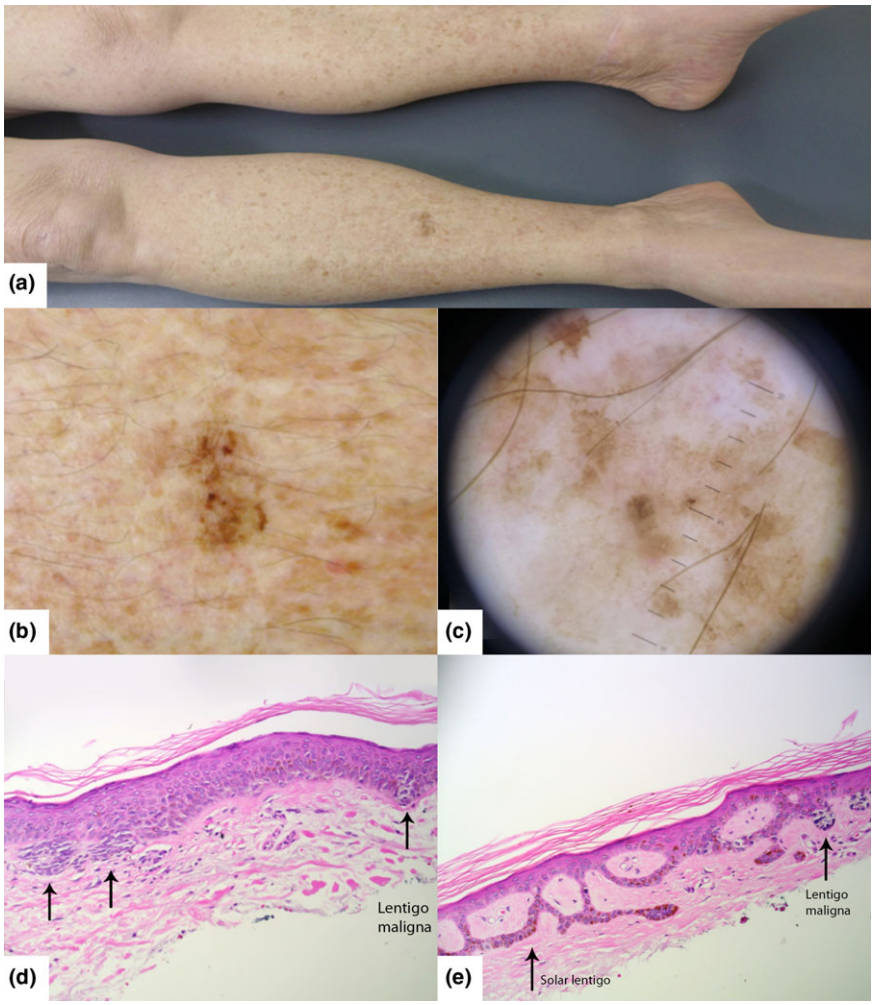

Figure 3 (a) Lentigo maligna arising in a solar lentigo. A large heavily pigmented stand-out lentigo-like lesion. (b) Close-up picture of lentigo maligna arising in a solar lentigo. (c) Dermoscopy of lentigo maligna arising in a solar lentigo demonstrating overall asymmetry, blue-grey areas, featureless areas, irregular network and broadened network. (d) Lentigo maligna arising in solar lentigo. Histology demonstrating the area of frank lentigo maligna. Random nests of melanocytes (arrows) connected by a confluent proliferation of basilar single melanocytes. (e) Histology of frank lentigo maligna (arrow) arising in solar lentigo (arrow).

maligna melanoma (LMM) and lentigo maligna *in situ* (LM) can be clinically and histologically difficult to define, the definition of adequate surgical treatment of the lesion poses another challenge.[10,12]

Solar lentigines have been described in association with melanoma *in situ* in patients with xeroderma pigmentosum (XP). Stern and colleagues described solar lentigo lateral to and contiguous with 14 of 16 melanomas arising in the context of XP. These solar lentigines underwent a gradual transition into melanoma *in situ* beginning with typical solar lentigo developing gradual sparse, benign-appearing melanocytes centrally increasing in number and in degree of atypia. These authors proposed that solar lentigines represent a precursor lesion for melanoma *in situ* in patients with XP. [13]

A melanoma precursor lesion is considered as one that is present prior to the development of a melanoma. Precursor lesions may be entirely benign or may be atypical, with some degree of malignant potential. Their presence places the patient at an increased risk of developing melanoma. Melanomas can arise in benign melanocytic lesions such as dysplastic naevi and congenital naevi. It is the opinion of the authors of the current article that lentigo maligna can arise within a solar lentigo: 'Having reported over one million patients and 1 450 000 specimens in the last 45 years I have seen several hundred cases of lentigo maligna arising in solar lentigos both on the face and the forearms', says David Weedon. The question of whether unstable solar lentigo is a precursor lesion for melanoma is not one that this article can answer. However, we believe that the unstable solar lentigo is a lesion that can occur in close juxtaposition to frank lentigo maligna or, if it is left in place, lentigo maligna can arise in these lesions over time. Whether this means an unstable lentigo is a precursor lesion, a transitional step or an epiphenomenon of lentigo maligna is unknown. Nevertheless, these lesions should be recognised and managed appropriately.

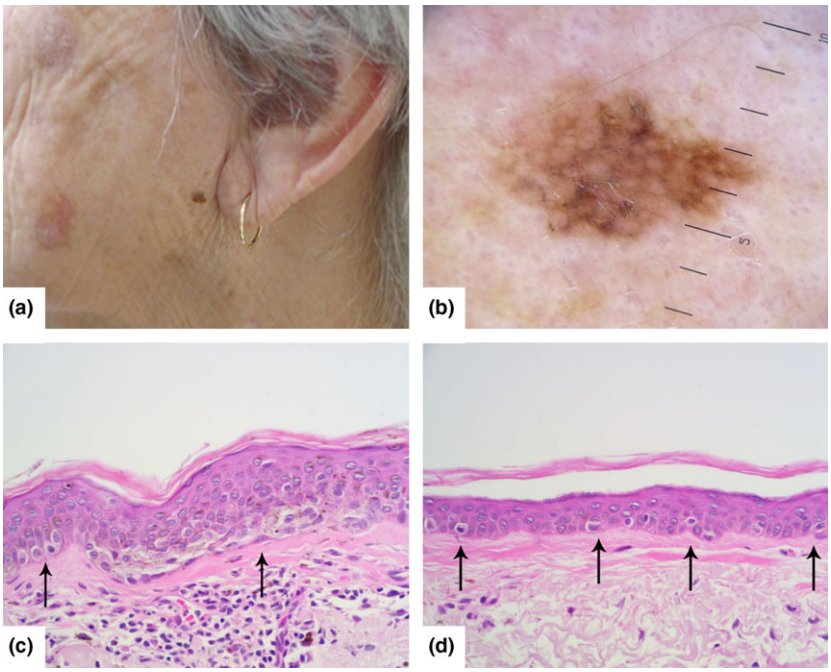

Figure 4 (a) Lentigo maligna arising in unstable solar lentigo. An isolated lentigo-like lesion. (b) Dermoscopy of lentigo maligna arising in unstable solar lentigo. Note the perifollicular pigment asymmetry, pseudo-network, rhomboidal structures and variety of colours, including light tan, dark tan and blue-grey. (c) Histology of a lentigo maligna arising in unstable solar lentigo. In the centre of the biopsy there are confluent nests of atypical melanocytes representing lentigo maligna (arrow). (d) Histology of a lentigo maligna arising in unstable solar lentigo. At the periphery there are increased numbers of normal melanocytes (arrows) representing solar unstable lentigo.

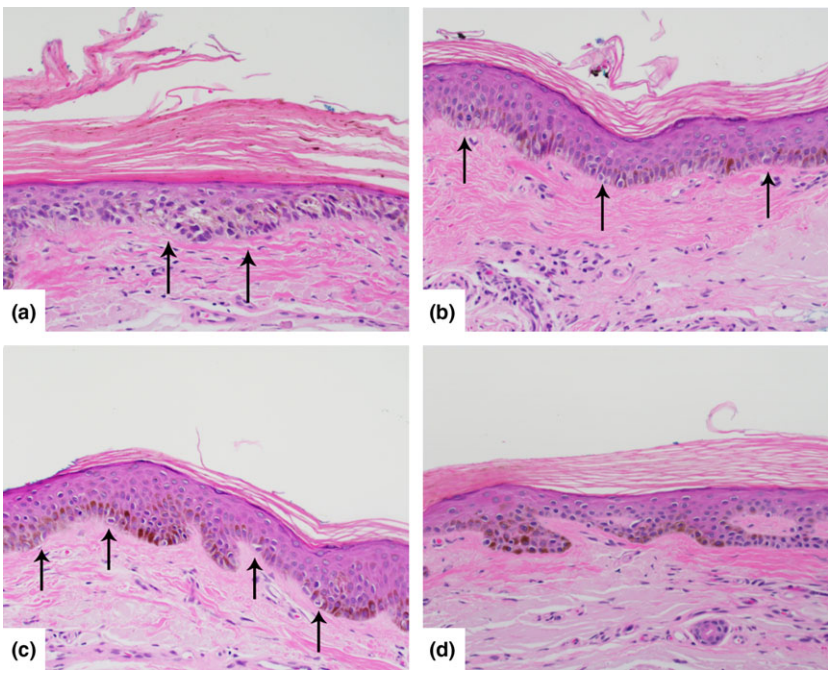

Figure 5 Histology demonstrating solar lentigo, unstable solar lentigo and lentigo maligna occurring within the one lesion. Note the progression from typical solar lentigo (periphery) to unstable solar lentigo to frank lentigo maligna (centre of lesion) within the one lesion. (a) Histology of centre of lesion demonstrating lentigo maligna. Note the confluent poorly formed nest of melanocytes (arrows). (b) Increased number of normal melanocytes (arrows) representing an unstable solar lentigo with solar elastosis. This section occurred adjacent to frank lentigo maligna (a). (c) Increased number of normal melanocytes (arrows) representing an unstable solar lentigo. This section occurred adjacent to frank lentigo maligna (a). (d) Histology of periphery of lesion demonstrating solar lentigo. This section was adjacent to the lentigo maligna and unstable solar lentigo (a–c).

LM is a malignancy of increasing incidence accounting for 4–15% of melanomas.[6] A recent population-based study in Queensland compared risk factors for LMM and superficial spreading melanoma.[14] Interestingly, they reported the strongest determinant for the development of LMM was the number of solar lentigines (OR 15.93, $P < 0.001$). However, number of naevi was not associated with the development of LMM. In contrast, risk for superficial spreading melanoma was related to the number of naevi and number of lifetime sunburns but not to the number of solar lentigines. The question may then be raised: if the presence of solar lentigines significantly increases the risk of development of LMM, and if LM arises in a solar lentigo, is there an intermediate precursor lesion?

The authors here reiterate Weedon's hypothesis [3] that the presence of melanocyte hyperplasia within a solar lentigo (unstable solar lentigo) may indicate a potential for it to evolve into LM in a process analogous to what Stern and colleagues observed in the XP population.[13] This hypothesis could reconcile some of the above observations; solar lentigines and LM occur in the same anatomical areas;[14] LM may evolve gradually out of long-standing solar lentigo lesions (Fig. 3); solar lentigo and unstable solar lentigo occur at the edge of LM (Fig. 5); and solar lentigo and LMM are linked demographically.[14]

We also recognize that we may be observing in some instances the spread of lentigo maligna into an adjacent solar lentigo. Technologies to distinguish the genetic abnormalities in such small cell samples are not readily available, nor are they probably necessary from a practical viewpoint; although, interesting studies have been carried out on the 'field cells' surrounding acral melanoma.[15] The gene amplifications characteristic of acral melanomas may be detected in the single basal melanocytes in the histologically normal appearing skin immediately adjacent to the melanoma. These field cells were interpreted as subtle surrounding melanoma *in situ*. Whether or not unstable lentigines can evolve into LM, we routinely encounter solar lentigo and unstable solar lentigo at the edge of LM (Figs 4,5). Similar studies on lentigo maligna and surrounding unstable solar lentigo would be of interest.

When confronted with a histopathology report documenting the presence of unstable solar lentigo it is the authors' practice to assess the patient. If a residual lesion is clinically evident then, where possible, the lesion is removed in its entirety. If complete removal is not possible further representative sampling of residual lesion may be required. Careful long-term follow up to allow earliest detection of lentigo maligna is undertaken if complete removal cannot be done.

CONCLUSION

Unstable solar lentigos usually present as irregularly pigmented macules on the background of chronic sun damage. They are often isolated lesions with a paucity of adjacent lentigines. Another common clinical presentation is of a lentigo-like lesion markedly different from its nearby fellows. A histologically unstable solar lentigo is characterised by melanocyte hyperplasia, with at most very mild melanocytic atypia, within a solar lentigo. Unstable solar lentigines may have malignant potential; however, evidence of this to date is anecdotal. Optimal management of these lesions is uncertain. It is the authors' current practice is to remove these lesions in their entirety. If this is impractical close observation and follow up is advised. The histopathological identification of this entity will permit ongoing research into its behaviour and thus appropriate management.

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