

Letter

Unknown primary melanoma

A recent and very interesting paper by Pavlidis *et al.* [1] on the diagnosis of unknown primary cancer stresses how difficult it is to manage these patients correctly.

In 2–6% of all patients suffering from metastatic melanoma, clinical examination of the skin and mucosa is not conducive to diagnosis of the primary tumour, which therefore remains unknown [1–4]. This matter is crucial in such cases, because there is no point in treating a metastatic lesion without eliminating the primary source of neoplastic cells.

Three theories have been proposed to explain the origin of metastatic melanoma from an unknown primary: the presence of a melanoma in anatomical sites that are not easily explored, the possible presence of ectopic melanocytes or the complete regression of the primary lesion. All of these occurrences have been reported in the literature [5–7].

Yet, in clinical practice, we very frequently see patients with metastases of an unknown primary melanoma who also have a large number of clinically unclassifiable pigmented lesions (possibly over 100). Moreover, suspicious lesions that have to be excised often fail to be identified by clinical examination, whether it be based on the ABCDE clinical criteria or on the so-called ugly duckling sign for melanoma detection [8]. The ‘ugly duckling’ sign is the presence of a naevus that does not clinically resemble its brother naevi. In patients with a large number of common and atypical naevi, a melanoma often has clinical features that are different from those of the other pigmented lesions, but not necessarily more impressive.

In these cases dermoscopy, which is not mentioned in Pavlidis *et al.*’ paper [1], may prove extremely useful both to single out a melanoma amongst the numerous other pigmented lesions as the origin of metastases, and to minimise the removal of clinically suspicious but histologically benign lesions.

Dermoscopy, also known as dermatoscopy and epiluminescence microscopy (ELM), is an *in vivo*, non-invasive technique that has disclosed a new dimension of the clinical morphological features of pigmented skin and mucosal lesions, thereby increasing the accuracy of diagnosis, as has been shown in recent years. It is indeed more specific than naked-eye examination alone [9], and effectively reduces the number of lesions to be excised.

Dermoscopy uses a surface microscope with incident-light magnification systems (incident light being delivered from an acute angle) and immersion oil at the microscope interface. The purpose of this method is to visualise numerous morphological features not visible to the naked eye, thereby improving the clinical diagnosis of nearly all pigmented lesions. The morphological features seen by ELM have specific, rather well-defined histopathological correlates. Investigators who know the histopathological equivalents of these features can increase the accuracy of *in vivo* diagnosis of melanocytic vs. non-melanocytic pigmented lesions and in particular of benign vs. malignant lesions. ELM can be performed with binocular stereomicroscopes, which provide a magnification range from 6× to 80×, and with a hand-held microscope equipped with an achromatic lens that reaches a fixed magnification of 10×.

Modern, advanced systems are at present available, thanks to the digital technology applied to ELM (D-ELM). This is a new integrated method based on advanced computer technology and image data processing (data acquisition, storage and retrieval). Currently available D-ELM camera systems can acquire, process, print and review clinical and ELM images in order to facilitate the follow-up of doubtful pigmented lesions [9,10].

This methodology enables us to distinguish melanocytic lesions, which are a potential risk and should therefore be followed up, from all the other benign non-melanocytic pigmented lesions that do not evolve, such as melanosis, seborrheic keratosis, venous haemangioma and postinflammatory pigmentation.

References

1. Pavlidis N, Briasoulis E, Hainsworth J, Greco FA. Diagnostic and therapeutic management of cancer of an unknown primary origin. *Eur J Cancer* 2003, **39**, 1990–2005.
2. Das Gupta T, Bowden L, Berg JW. Malignant melanoma of unknown primary origin. *Surg Gyn Obstet* 1963, **117**, 341–345.
3. Velez A, Walsh D, Karakousis CP. Treatment of unknown primary melanoma. *Cancer* 1991, **68**, 2579–2581.
4. Chang AE, Karnell LH, Menck HR. The national cancer data base. Report on cutaneous and noncutaneous melanoma. A summary of 84,836 cases from past decade. *Cancer* 1998, **83**, 1664–1678.
5. De Matos P, Tyler DS, Seigler MF. Malignant melanoma of the mucous membranes: a review of 119 cases. *Ann Surg Oncol* 1998, **5**, 733–742.

6. Ridolfi RL, Rosen PP, Thaler H. Nevus cell aggregates associated with lymph nodes: estimated frequency and clinical significance. *Cancer* 1977, **39**, 164–171.
7. Pellegrini A. Regressed primary malignant melanoma with regional metastasis. *Arch Dermatol* 1980, **116**, 585–586.
8. Grob JJ, Bonerandi JJ. The “ugly duckling” sign: identification of the common characteristics of nevi in an individual as a basis for melanoma screening. *Arch Dermatol* 1998, **134**, 103–104.
9. Carli P, De Giorgi V, Soyer HP, et al. Dermatoscopy in the diagnosis of pigmented skin lesions: a new semiology for the dermatologist. *J Eur Acad Dermatol Venereol* 2000, **14**, 353–369.
10. De Giorgi V, Carli P. Epiluminescence microscopy of pigmented skin lesions. In Katsambas AD, Lotti TM, eds. *European handbook of dermatological treatments*. Berlin, Springer, 1999, pp 668–674.

Vincenzo de Giorgi
Marcello Stante
Paolo Carli
Department of Dermatology
University of Florence
Via degli Alfani 37
50121 Florence
Italy
E-mail addresses: vdegi@tin.it; dermoncologia@unifi.it
(V. de Giorgi)

Received 16 February 2004; Accepted 19 February 2004

Available online 6 May 2004