Editorial

Diagnosis of thin melanoma

The past few decades have witnessed a marked increase in the incidence of cutaneous melanoma, especially of the thin presumably "early" melanomas. This, together with the identification of a number of benign melanocytic tumours which resemble melanoma, as well as a variety of "naevoid melanoma" types, results in an ever increasing number of diagnostic problem cases, a significant proportion of which are small and thin lesions.

The CRC Melanoma Pathology Panel study reported by Cook and colleagues, which appears in this issue,[1] is a major effort to measure the reproducibility of the distinction between melanoma and naevi in a series of problematic thin lesions. The study was performed not only by a group of experts with a special interest in the field but also by a group of randomly selected diagnostic histopathologists. In this respect, this highly interesting study represents a major advance in the assessment of the quality of histopathological diagnosis or, perhaps, the limits of what we have thus far achieved.

No doubt there are limits to what we can currently achieve in the distinction between thin melanoma and benign melanocytic tumours. Some, but by no means all, interobserver variability probably relates to differences in personal experience. However, significant intrinsic problems in diagnosis, not related to individual pathologist's performance, remain to be solved.

An important problem relates to the exceedingly favourable prognosis of thin melanoma in the absence of the so-called "vertical growth phase"—such lesions practically never metastasise. Accordingly, it is reasonable to question whether such lesions are really fully malignant tumours, whether some are melanoma simulators or, perhaps, melanoma precursors, which have not yet attained a fully malignant phenotype. Indeed, follow up data indicate that the emergence of clinically relevant (potentially life threatening) melanoma is not associated with the penetration of the epithelial basal lamina, but rather with the emergence of the vertical growth phase, hallmarked histologically by a number of features, the most important of which are the presence of intradermal nests larger than the largest intraepidermal nest, and intradermal mitoses.[2] Elder and Murphy remarked that "the cells of the vertical growth phase probably represent a subclone derived by tumor progression from the radial growth phase cells".[3] Together, these data and considerations suggest that radial growth phase melanoma may in fact be a premalignant lesion rather than a true fully fledged melanoma.

An additional problem relates to the fact that melanomas arising in naevi do not necessarily arise from a (transformed) intraepidermal melanocyte; most often, the precursor lesion has already spread to the dermis and the intradermal component does not consist solely of postmitotic end cells. Therefore, it is not logical to assume that there is an obligatory in situ melanoma phase preceding the invasive melanoma. Some melanomas may well be invasive ab initio and may even involve the epidermis secondarily, a phenomenon demonstrated conclusively to occur in some cutaneous metastases of melanoma.[4] Obviously, the sequence of events in malignant transformation and spread of transformed melanocytes is essentially different from that in epithelial neoplasia, where infiltrative carcinoma is preceded by malignant transformation of a cell within the epithelial compartment (carcinoma in situ).

Additional indirect evidence arguing against a concept of in situ melanoma as the obligatory direct precursor of invasive melanoma was presented by Moore *et al.*[5] This group conducted a population screening study and found that prevalence of clinical melanoma risk factors (hair colour, eye colour, skin type, tendency to develop sunburn, ability to tan) differed from the control group in patients with invasive melanoma, but not in those with in situ melanoma.

These problems have a direct bearing on the concept of MIN (melanocytic intraepidermal neoplasia). Involvement of dermal connective tissue does not appear to equate with invasion in the classical sense of epithelial neoplasms. In addition, the intraepithelial melanocytic lesion often extends from the epidermis into the adnexal epithelium, especially of the hair follicles, so that "intraepithelial" would be preferable to "intraepidermal". The use of the term MIN as a synonym for melanoma in situ as well as all severely dysplastic junctional *or compound* lesions[6] appears to increase the potential confusion. Finally, since benign naevi are, in all likelihood, also neoplasms, the term MIN would also be applicable to (junctional) naevi, which is clearly not the intention. For these reasons, I fear that the term MIN has significant conceptual and practical drawbacks.

In conclusion, diagnostic pathologists find themselves confronted with increasing numbers of small melanocytic tumours with histological features bearing some, or a close, resemblance to (usually larger) melanomas, but which carry a very good prognosis. The distinction between benign and malignant lesions cannot be made with certainty in a number of these cases. Only part of this lack of success is due to suboptimal performance of the individual pathologist. The concept of an obligatory in situ phase of melanoma is conceptually flawed and, indeed, the emergence of clinically significant melanoma appears to be related to a number of features of the intradermal tumour component, rather than the mere extension into the dermal tissue. Obviously, important issues remain to be solved and no matter how expert the experts are, there will be some interobserver variability. Indeed, modesty dictates that at present the final verdict in a number of such cases will be no more than a—moderately reproducible—"favoured diagnosis". It is the considerable merit of the study conducted by the CRC Melanoma Pathology Panel to have provided quantitative data on interobserver variation in this problem-ridden area of diagnostic pathology.

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1 Cook MG, Clarke TJ, Humphreys S, Fletcher A, McLaren KM, Smith NP, *et al.* CRC Melanoma Pathology Panel. A nationwide survey of observer

variation in the diagnosis of thin cutaneous malignant melanoma including the MIN terminology. *J Clin Pathol* 1997;**50:**202–5.
2 Clark WH Jr, Elder DE, Guerry D IV, Braiteman LE, Trock BJ, Schultz, *et al*. Model predicting survival in stage I melanoma based on tumor progression. *J Natl Cancer Inst* 1989;**81:**1893–904.
3 Elder DE, Murphy GF. *Melanocytic tumors of the skin*. Washington: Armed Forces Institute of Pathology, 1991:128.
4 Abernethy JL, Soyer HP, Kerl H, Jorizzo JL, White WL. Epidermotropic metastatic malignant melanoma simulating melanoma in situ. A report of 10 examples from two patients. *Am J Surg Pathol* 1994;**18:**1140–9.
5 Moore DH, Schneider JS, Sagebiel RW. Discordance of risk factors for invasive and non-invasive melanoma [letter]. *Lancet* 1990;**335:**1523–4.
6 Cook MG, Clarke TJ, Humphreys S, Fletcher A, McLaren KM, Smith NP, *et al*. The evaluation of diagnostic and prognostic criteria and the terminology of thin cutaneous malignant melanoma by the CRC Melanoma Pathology Panel. *Histopathology* 1996;**28:**497–512.