

Naevus or melanoma? An inadequate paradigm for a small number of clinically important lesions

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The large majority of melanocytic proliferations undergoing excisional biopsy are easily classified as benign melanocytic naevi or malignant melanoma by routine histological examination. However, there is a small group of lesions that do not easily fit this dichotomous approach.¹ This is unsurprising, as histological diagnosis involves the subjective identification and interpretation of multiple, and sometimes disparate architectural and cytological features, almost all of which individually show an imperfect relationship with the true biological nature of a neoplasm. Broadly, these problematic melanocytic lesions fall into two (sometimes overlapping) groups:

- Lesions that have conflicting morphological criteria, rendering it difficult to decide whether the lesion is a bona fide melanoma or a benign naevus with atypical histological features of limited biological import.² Some examples of the numerous diagnostic labels that may be applied to such lesions include severely dysplastic naevus, early/evolving melanoma arising in dysplastic naevus, superficial atypical melanocytic proliferation of uncertain significance, and atypical Spitz tumour/naevus.
- Lesions that have a truly intermediate biological potential, in many cases with a surprisingly high rate of spread to

regional lymph nodes, but infrequent widespread dissemination, and a prognosis much better than that of conventional melanoma with similar staging attributes.³ Some examples of nomenclature that can be used for such lesions include atypical Spitz tumour/spitzoid tumour of uncertain malignant potential, spitzoid melanoma of childhood, melanocytic tumour of uncertain malignant potential, and atypical cellular blue naevus.

There is an understandable tendency among some clinicians to regard an 'uncertain' diagnosis with a degree of anxiety or scepticism. There may be concern that such an interpretation reflects a lack of pathological expertise or a belief that another practitioner may render a more definitive interpretation. In this scenario, it is important not to conflate diagnostic certainty with diagnostic accuracy. While expert consultation is valuable, and almost invariably sought, there is ample evidence that even among experts, there is very significant inter-observer variability in the interpretation of lesions in these difficult groups.⁴ Furthermore, biological outcome is not always accurately predicted by even a large 'majority' opinion; that is, malignant clinical behaviour can be observed in lesions considered to show benign features by a preponderance of experts and vice versa.⁴

Pressure sometimes arises to label a lesion as malignant if there is any uncertainty. The rationale for this is understandable – a malignant diagnosis cannot be proven wrong, as a good outcome can be attributed to the efficacy of treatment, whereas an adverse outcome after a benign diagnosis proves error. However, it is clear that in recent decades, there has been a degree of pathological over-diagnosis of melanoma.⁵ Over-diagnosis and over-treatment are associated with multiple costs that do not require reiteration here.

Secondly, because such uncertain diagnoses are infrequent, many practitioners will have limited experience with this group of lesions. The clinician may perceive a difficulty in explaining the diagnosis and its significance to the patient or in determining how to manage such a lesion. A detailed discussion of the management approach is beyond the scope of this article; however, a few simple principles deserve mention.⁶ For all lesions that fall into an 'uncertain' category, therapeutic excision with histologically clear margins is the mainstay of management. For lesions that are entirely intra-epidermal, and for the large majority of 'thin' lesions (<1 mm thick), complete excision will be curative, regardless of the 'true' biological diagnosis. Following complete excision, patients in this group can be reassured and followed up clinically, most importantly

for the development of separate and potentially more significant melanocytic lesions. For thicker lesions, where discussions of more extensive resection, sentinel lymph node biopsy or more aggressive monitoring may be an issue, management by a multidisciplinary team with experience in this field is appropriate. A frank discussion of these issues with patients is possible, typically well received and necessary for informed consent.

There has been significant work in recent years to reduce the (already small) number of lesions for which prediction of biological potential is difficult. These include the use of fluorescence in situ hybridisation (FISH) testing or comparative genomic hybridisation, which are currently in clinical use, to assess genetic copy number variation. It is likely that these adjunctive tests will be supplemented in the near future by sequencing-based approaches. However, we should not expect that these tests will entirely eliminate a group of lesions of uncertain biological potential. Indeed, it is becoming increasingly clear that lesions that are difficult to classify under the microscope show intermediate genetic abnormalities, in some cases representing partial progression in a multistep pathway.⁷

In conclusion, we would like to emphasise that mature clinical practice requires an understanding that a simplistic benign versus malignant concept of pathological diagnosis fails to entirely encompass the difficulties of morphological interpretation or the biological complexities of human melanocytic pathology. Uncertain diagnoses in melanocytic pathology are an infrequent but well-studied occurrence. The appropriate clinical approach to this scenario is established. Such diagnoses do not represent a lack of diagnostic competence and do not present an insuperable barrier to appropriate communication with, or management of, the patient. In all such cases, consultation with an experienced dermatopathologist and/or an appropriate multidisciplinary team will lead to development of an appropriate management plan and, possibly, to mitigation of anxiety for the patient and primary care physician.

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