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MELANOCYTIC TUMOUR PATHOLOGY

The regenerating naevus

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Summary

The re-emergence of a melanocytic proliferation at the site of a previously excised pigmented lesion may not only cause great concern clinically but may also be amongst the most difficult of all melanocytic lesions for pathologists to assess. These lesions can adopt an appearance which may be impossible to confidently distinguish from a regressing or traumatised melanoma on histological grounds alone. For this reason, careful attention must be paid to the clinical context which has given rise to the lesion or a misdiagnosis may occur. In the absence of a corroborating history of prior surgery or trauma to the site, a diagnosis of a regenerating naevus may only be provisional. When considering a diagnosis of regenerating naevus, whenever possible, it is important to review and confirm the benign nature of the precursor lesion. Nevertheless, 50 years of research into this phenomenon has identified certain characteristic clinical features and histological patterns which provide clues both to clinicians and pathologists that will assist them to make the correct diagnosis and avoid over diagnosing as melanoma what is ultimately a benign process.

Key words: Diagnosis; pathology; melanoma; persistent naevus; pseudomelanoma; regenerating naevus; recurrent naevus.

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INTRODUCTION

The regenerating naevus is recognised as a potential diagnostic pitfall in melanocyte pathology.[1–3] Repigmentation at the site of a partially or completely excised naevus can generate considerable concern for patients as well as clinicians and the presence of a melanocytic proliferation at the site of a previously excised pigmented lesion may cause diagnostic uncertainty for pathologists. These uncommon lesions are particularly prone to pathological misdiagnosis in partial biopsy specimens, especially when they are examined without knowledge of pertinent clinical information, for their histopathological appearance can show considerable overlap with regressing melanomas.

The phenomenon of recurrent naevi has long been recognised,[4] but the capacity of trauma to induce junctional melanocyte 'activation', and thus regeneration and hyperplasia, was first systematically studied by Cox and Walton.[5] They analysed the changes in cellularity between initial biopsies and re-excision specimens and noted that in up to 56% of patients' re-biopsies, naevi exhibited a degree of junctional melanocyte hyperplasia which exceeded that observed in the original naevus. Although the authors highlighted that an understating of the nature of trauma-induced stimulated junctional activity can help inform subsequent surgical management, it was left to the work of Ackerman and Kornberg[6] and Reed and colleagues[7] to highlight the capacity for this phenomenon to mimic melanoma. Ackerman and Kornberg documented a series of eight patients with rapidly recurring pigmented lesions following incomplete excision that displayed common histological features which could, if assessed in isolation, lead to misdiagnosis of melanoma for what they proposed was a benign process. Of most concern pathologically was the presence of histological features which overlap with those found in superficial spreading melanoma *in situ*; a hypercellular proliferation of junctional melanocytes with a greatly variable nested and single cell growth pattern, occasional confluent growth as well as some cytological atypia and, in particular, the presence of pagetoid spread. The latter may be particularly florid within regenerating naevi. They counselled that although there are features which are helpful in avoiding over-diagnosing these lesions as melanoma, namely the presence of sharply circumscribed borders, absence of necrosis, rarity of mitoses, invariable subjacent often scar-like dermal fibrosis and the recognition of dermal naevus remnants, the most important thing to remember was that 'only accurate review of the original biopsy specimen can confirm with certainty the benign nature of the original neoplasm'. Their observations and advice remain relevant to this day.

The label 'pseudomelanoma' has been controversial since its inception.[8] Although the term alerts the diagnostician to the need for vigilance in avoiding over diagnosing these lesions as melanoma, pseudomelanoma continues to be used to identify non-melanocytic lesions which clinically simulate melanoma.[9–12] Regenerating naevus, recurrent naevus and

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Table 1 Summary of studies assessing naevus recurrence rates

Study	Naevi	Method of removal	Margin involvement	Minimum follow up	Recurrence rate
Bong *et al.*[13]	83	Shave, 100%	NA	12 months	27%
Ferrandiz *et al.*[14]	204	Shave, 100%	64%	3 months	19.6%
Gambichler *et al.*[15]	77	Shave, 100%	12%	6 months	13%
Goodson *et al.*[16]	246	Shave, 60.1% Punch, 27.3% Excision, 16.6%	52.0%	24 months	2.8%
Tallon *et al.*[17]	1035	Shave, 12.4% Punch, 9.9% Excision, 74.5% Other, 3.3%	26.3%	60 months	0.3%[a]

NA, not assessed.
[a] Recurrence rate calculated from laboratory database.

persistent naevus are used interchangeably in the literature and, in the authors' opinion, all represent more appropriate terms than pseudomelanoma, because not all regenerating naevi pose diagnostic difficulty for the pathologist but they are all the result of the benign proliferation of naevocytes at the site of trauma.

CLINICAL FEATURES

The incidence of regenerating naevi varies considerably in the literature. Method of excision and thus likelihood of margin involvement, as well as clinical follow up and the method of assessing for the presence of recurrence (i.e., clinical examination alone or histopathological confirmation) has differed between the various studies on the subject and correspondingly the rate of recurrence varies from 0.3% to 27% (Table 1). However, it is apparent that amongst the case series with higher proportions of shave biopsies, the rate of recurrence is higher.[13–17]

Regenerating naevi display characteristic clinical features (Table 2). They are reported to occur more frequently in females and young patients.[18–20] The back is commonly cited as the body region most likely to give rise to a recurrence.[1] Some have proposed that this is could be a function of a thicker dermis being more likely to harbour residual naevocytes,[20] while others contend this reflects the general distribution of biopsied naevi.[21] The reported rate of involvement of the margins by naevus cells in the primary excision is typically high.[17] Most regenerating naevi arise from common acquired naevi, followed by dysplastic naevi and congenital naevi[12] (Table 2). Recurrences in specialised naevi such as Spitz naevus[22] or blue naevi[23] are considered to be uncommon events but this probably reflects the prevalence of these tumours. Regenerating naevi usually recur rapidly, most commonly within 6 months and almost always within 12 months of the prior biopsy or traumatic event, although we have seen cases of late recurrence of naevi confirmed on review of the prior specimen and subsequent long-term clinical follow-up.

The clinical presentation is variable but some recurring patterns have been described. Recurrent naevi typically break the common clinical rules of benignity, displaying asymmetry, irregular borders and variegated colouration. Other common dermoscopic features include radial lines and a centrifugal growth pattern.[24–26] Recurrent naevi are characteristically strictly macular lesions,[6] but recurrent blue naevi[23] and Spitz naevi[22] are notable exceptions. In a dermoscopic comparison of 98 recurrent naevi and 62 recurrent melanomas, Blum *et al.* demonstrated features such as a circular pattern, eccentric hyperpigmentation, chaotic, non-continuous growth and extension beyond the scar were patterns more commonly, but not exclusively, encountered in melanoma.[25]

Table 2 Summary of studies assessing the clinical features of recurrent naevi

	King *et al.*[18] 354 cases	Sommer *et al.*[20] 205 cases	Park *et al.*[19] 175 cases
Female	72%	65%	85%
Median age (range)	30 (7–92)	'most between 25-50 years' (6–88)	'most…between 20–30 years' (3–76)
Site			
Head and neck	6%	10%	26%
Chest/Abdomen	20%	15%	'Trunk' (54%)
Back	57%	49%	–
Extremities	16%	24%	16%
Precursor naevus			
Common acquired	64%	26%	NA
Congenital	6%	NA	NA
Dysplastic	28%	72%	NA
Other	1%	1%	NA
Original naevus with involved margins	77%	75%	97%
Median months to recurrence (range)	5 (1–63)	'most biopsied <6 months'	4.75 (1–216)

NA, not assessed.