Melanoma arising in a persistent nevus: Melanoma where 'pseudomelanoma' is expected

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Key words: dysplastic nevus; genomic testing; melanoma; observation; persistent nevus; precursor; pseudomelanoma; recurrent nevus.

INTRODUCTION

The risk of melanoma arising from Clark (dysplastic) nevi, simple lentigines, or junctional nevi is small, with melanoma estimated to arise in about 1 in 10,000 Clark nevi.[1] Because of this low risk, clinicians may opt to hold off on additional removal for nevi with histologic margin involvement.[2,3] If a lesion recurs, diagnostic difficulties in histological interpretation may arise.[4] Persistent nevi may exhibit histologic features that can mimic melanoma.[4,5] Inexperienced pathologists may attribute features of melanoma as changes due to "persistent nevus effect". We report a case of melanoma arising in the setting of a persistent nevus to illustrate potential pitfalls and the value of genomic confirmation.

CASE REPORT

A 33-year-old pregnant woman with an enlarging periumbilical pigmented lesion had a biopsy 16 months earlier, which was found to be benign (Fig 1). The area had healed well without a clinically apparent residual lesion only to recur during her pregnancy. She presented for evaluation at which time examination revealed an asymmetric pigmented lesion extending beyond scar. The clinical impression was of a "growing persistent nevus". Excisional biopsy revealed nevus, scar, and melanoma (Figs 2, 3, and 4). Proliferation of single melanocytes in a pagetoid pattern was noted above the scar and extending beyond the scar. Atypical melanocytes extended into the dermis. The melanoma had a Clark level IV, a Breslow thickness of 0.8 mm, and 1 mitosis per mm^2. Perineural and lymphatic invasion were not identified, nor was regression noted. A 23-gene expression profile provided a numerical score of 6.5 (classified as malignant). She underwent evaluation at a National Cancer Institute comprehensive melanoma care center where the diagnoses of the initial biopsy and excisional biopsy were confirmed. Subsequent wide excision with a conventional margin for invasive melanoma (T1b) was performed, and the patient continues to do well 4 years later.

DISCUSSION

Identifying best practices for the management of nevi is complicated by differences in risk tolerance. Some clinicians routinely perform tangential biopsies and partial biopsies of nevi. When pigmented lesions are not removed in their entirety, clinicians may assume that the recurrent or persistent lesion will likely exhibit the same features as the initial specimen. Dysplastic nevi may pose a particular challenge. As clinicians try to avoid "overtreatment", a subset of biopsied lesions may recur. Observation is a reasonable management approach for moderately dysplastic nevi excisionally biopsied but with positive histologic margins; however, there is a need for continued monitoring of patients.[2,3] Most nevi do not recur and no further treatment is needed. The same holds true for dysplastic nevi. Although most pigmented lesions diagnosed as dysplastic nevi are merely markers of melanoma risk rather than melanoma precursors, an undefined and probably small subset of precursor lesions that do not meet the

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Funding sources: None.
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JAAD Case Reports 2021;12:5-7.
2352-5126

https://doi.org/10.1016/j.jdcr.2021.03.045

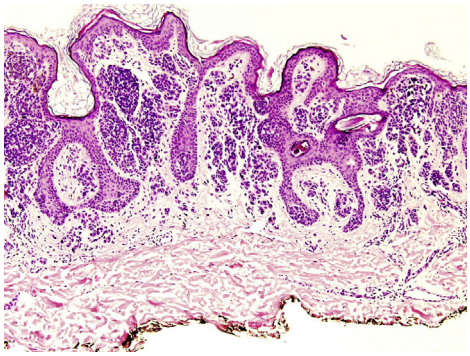

Fig 1. The initial biopsy revealed a banal nevus devoid of inflammation, expansile nests, or atypical features. (Hematoxylin-eosin–stain; original magnification, ×100.)

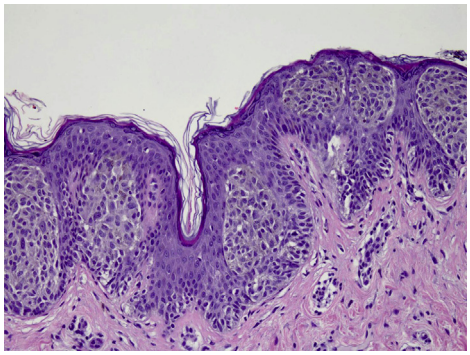

Fig 2. Excisional biopsy revealed well-circumscribed nests consistent with persistent periumbilical nevus. (Hematoxylin-eosin–stain; original magnification, ×200.)

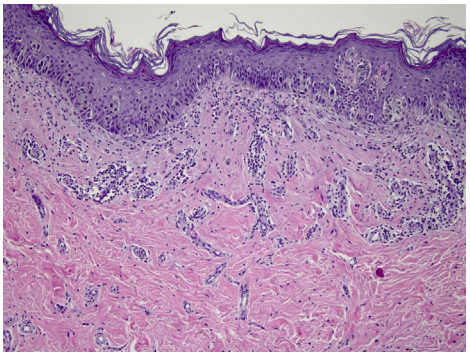

Fig 3. Proliferation of single melanocytes and pagetoid spread were prominent over the scar in a pattern reminiscent of persistent (recurrent) nevus. A few atypical melanocytes were noted in the dermis. (Hematoxylin-eosin–stain; original magnification, ×100.)

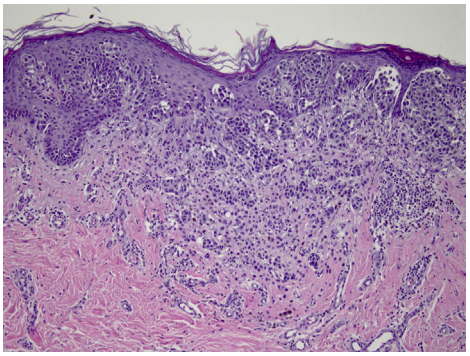

Fig 4. Atypical melanocytes with enlarged and hyperchromatic nuclei were observed to invade into the dermis to a depth of 0.8 mm. Lymphocytes surrounded dermal melanocytes, and pigment was distributed in an irregular fashion. (Hematoxylin-eosin–stain; original magnification, ×100.)

histologic criteria for melanoma end up being categorized as dysplastic nevi and have the potential to evolve into a melanoma. Genomic models of progression support this possibility, and a recent report provides a practical example, where a melanocytic proliferation meeting the criteria of a nevus developed into melanoma through acquisition of genetic aberrations with ultraviolet signature.[6,7] Many dermatopathologists have encountered situations where melanoma is found upon re-excision of a nevus.[8,9] In some cases, this may be the result of an error in the original diagnosis.[10] In other cases, this may represent progression to melanoma and can be encountered in virtually any type of melanocytic proliferation. Longitudinal follow-up has even identified cases of melanoma arising in the setting of solar lentigines.[11-13] Correlation of clinical findings with genomic studies promises to refine our current paradigms, diagnostic criteria, and improve routine classification and management.

One could argue that the initial biopsy in our patient missed a small focus of melanoma or that genetic alterations were already present at the time rather than arising later in the persistent nevus component. It is impossible for us to refute those possibilities, but from a practical standpoint, those issues are not relevant to the challenge faced by clinicians each day. Clinicians must remain aware that melanoma can arise in an area where a previous biopsy was diagnosed as a nevus. The dermatopathologists who reviewed the specimens concurred with the diagnosis of nevus on the initial specimen and with melanoma arising in a nevus on the excisional specimen, as the histologic criteria were met.[14,15] The genomic test used to confirm the diagnosis in this case has a specificity of about 96%.[16] The melanoma arose in the exact location where the nevus had been removed by tangential biopsy more than a year earlier and was in a location easily monitored by the patient.

The willingness to attribute unusual features to "special site", pregnancy, and "persistent nevus effect" can cause diagnostic difficulties. Although

atypical histologic features are frequently associated with persistent nevi,[4,5] concurrent melanoma should always be considered. Pregnancy and special sites have been associated with unusual histologic features, but invasion into the dermis by atypical melanocytes, the presence of dermal mitoses, and the overall architecture allow for a confident diagnosis. Our case illustrates why pregnancy should not delay biopsy of an atypical lesion. Dermoscopic evidence of extension of melanocytic proliferation beyond a scar is a useful clue, which can help clinicians decide which lesions are at high risk.[17] Genomic testing can support a diagnosis for ambiguous lesions or help bring more certainty to an emotionally charged situation, such as in the case reported here. Although melanoma arising in association with a persistent nevus is rare, clinicians should be careful to recommend follow-up evaluation, especially if a lesion recurs, or if a persistent lesion changes.

Conflicts of interest

None disclosed.

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