The utility of re-excising mildly and moderately dysplastic nevi: A retrospective analysis

Lauren Strazzula, BA,[a] Priyanka Vedak, BA,[a] Mai P. Hoang, MD,[b] Arthur Sober, MD,[a] Hensin Tsao, MD, PhD,[a] and Daniela Kroshinsky, MD, MPH[a]
Boston, Massachusetts

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Background: The management of dysplastic nevi (DN) is a highly debated and controversial topic within the dermatology community. Clinicians agree that margin-positive severely DN should be removed with a surgical margin, however, there is disagreement surrounding the appropriate management of margin-positive mildly and moderately DN.

Objective: We sought to evaluate the utility of re-excising margin-positive mildly and moderately DN.

Methods: A retrospective chart review was conducted on all adult patients given the diagnosis of a biopsy-proven DN from 2010 through 2011. The primary outcomes were defined as the presence of melanocytic residuum in re-excisional specimens and a clinically significant change in diagnosis.

Results: A total of 1809 mildly and moderately DN were diagnosed from 2010 through 2011. In all, 765 (42.3%) of these lesions were found to have positive surgical margins during biopsy, and 495 (64.7) of the 765 lesions were subsequently re-excised. Melanocytic residuum was present in 18.2% of re-excisional specimens. Re-excision resulted in a clinically significant alteration of the diagnosis in only 1 case (0.2%).

Limitations: Limitations include retrospective design and inability to assess for malignant transformation given limited follow-up.

Conclusions: Re-excising mildly and moderately DN results in a low histopathological yield and rarely results in a clinically significant change in diagnosis. As such, clinical monitoring of margin-positive lesions may be warranted. (J Am Acad Dermatol 2014;71:1071-6.)

Key words: dermatopathology; dysplastic nevus; melanoma; nevus; pigmented lesions; surgical management.

The concept of the dysplastic nevus (DN) was first described in 1978 by both Clark et al[1] and Lynch et al[2] in 2 separate publications describing a phenotypic syndrome in melanoma-prone families. The term "dysplastic nevus" itself was introduced 2 years later[3] and these publications classified the DN as a premalignant lesion.[1-3] In recent years, this very notion has become controversial in the dermatology and dermatopathology communities,[4-6] and ambiguity continues to exist surrounding the possible progression of these lesions to melanoma. The concept that the DN may represent a premalignant lesion is further propagated by the fact that many pathologists grade the atypia found in DN from mildly to severely dysplastic based on histopathological criteria. As a result of the continued debate within the scientific community surrounding the biological behavior of DN, there are

From the Departments of Dermatology[a] and Pathology,[b] Massachusetts General Hospital.
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Reprint requests: Daniela Kroshinsky, MD, MPH, Department of Dermatology, Massachusetts General Hospital, 50 Staniford St, #200, Boston, MA 02114. E-mail: dkroshinsky@mgh.harvard.edu.
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no uniformly accepted guidelines to aid clinicians with the management of these lesions.

Currently the majority of clinicians agree that all severely DN should be re-excised with appropriate surgical margins[7]; however, data suggest that there is disagreement among dermatologists managing mildly or moderately DN, and the decision to re-excise is highly influenced by the involvement of surgical margins during initial biopsy.[7,8] According to a recent survey, 9% of respondents agreed that they would re-excise a moderately DN with clear margins versus 81% of individuals who would re-excise moderately DN with positive margins.[7]

In clinical practice, the pathology of a re-excised margin-positive mildly and moderately DN often shows dermal scar rather than residual atypical nevus.[9-12] DN are among the most common conditions treated in the dermatology clinic. As such, the treatment of these challenging lesions is both time-intensive and costly. In the current health care climate, there is ever-growing focus on improving the quality of health care while minimizing unnecessary costs. In this study, we sought to investigate the utility of re-excising mildly and moderately DN based on the prevalence of melanocytic residuum in incompletely excised lesions.

CAPSULE SUMMARY

- The management of mildly and moderately dysplastic nevi varies among physicians.
- Re-excising margin-positive mildly and moderately dysplastic nevi yielded melanocytic residuum in only 18% of cases, with a clinically significant change in diagnosis in only 1 of 495 patients.
- Given these results, clinical monitoring of margin-positive mildly and moderately dysplastic nevi, rather than re-excision, may be considered.

METHODS

This study was approved by the Partners Institutional Review Board. A retrospective chart review was conducted using the Research Patient Data Registry on all adult patients seen at Massachusetts General Hospital Dermatology Associates from January 1, 2010, through December 31, 2011, using the search terms "nevus," "blue nevus," "neoplasm of uncertain behavior," "pigmented nevus of skin," and "biopsy." All biopsy-proven DN were included for review. Any biopsy that was performed for "sampling" purposes rather than clinical clearance was excluded. Patient demographics, size of lesion, location of lesion, method of biopsy, type of nevus, degree of cytologic atypia, involvement of surgical margins, and method of re-excision were all recorded. Positive surgical margins were defined as residual atypical melanocytes present at inked margins. Degree of dysplasia was graded using the University of Pennsylvania criteria[13] during routine clinical care.

The primary outcomes were defined as the presence of residual melanocytes in re-excisional specimens and a clinically significant change in diagnosis (defined as an upgrade in degree of atypia from mildly or moderately dysplastic to severely dysplastic or melanoma). Two lesions received a clinically significant upgrade in diagnosis during re-excision. These 2 lesions were re-reviewed by a dermatopathologist (M. P. H.) who was blinded to the original biopsy and re-excision diagnoses. Eighteen additional lesions in the melanocytic residuum group were randomly selected using a computerized randomization tool and also re-reviewed by the blinded dermatopathologist (M. P. H.) as controls. The χ^2 test was applied to compare proportions, and the t test was applied to compare means. Statistical significance was defined as P less than .05.

RESULTS

From 2010 through 2011, 2084 DN were biopsied at Massachusetts General Hospital. Of these, 1809 (86.8%) were diagnosed as mildly and moderately DN, and 765 (42.3%) of the mildly and moderately DN were classified as having atypical melanocytes extending to the margin. Older patients, patients with a history of melanoma, lesions on the lower extremity, junctional nevi, and mildly DN were found in larger proportions in the negative margin group whereas larger lesions, lesions on the head and neck, compound nevi, moderately DN, and nevi exhibiting features of congenital onset were more commonly observed in the margin-positive group (Table I) ($P < .05$). Nine percent of margin-negative lesions were initially removed via fusiform excision versus 2.2% of margin-positive lesions ($P < .001$); however, there was no statistically significant difference in lesion clearance when examining punch biopsy specimen versus shave removal ($P > .05$).

A total of 495 (64.7%) of the 765 margin-positive lesions were subsequently re-excised. In all, 405 (81.8%) of re-excisional pathology specimens showed dermal scar whereas 90 (18.2%) of specimens contained residual atypical nevus (Table II). Lesions that were diagnosed as compound nevi during initial

Table I. Characteristics of biopsied mildly and/or moderately dysplastic nevi

	Biopsy positive margins, N = 765 (42.3%)	Biopsy negative margins, N = 1044 (57.7%)	*P* value
Male, n (%)	296 (38.7)	418 (40.0)	.563
Mean age, y	42.6	45.7	<.001
History of MM, n (%)	84 (11.0)	155 (14.9)	.016
Mean lesion size, mm	5.14	4.66	<.001
Location, n (%):			
Head and neck	47 (6.14)	14 (1.34)	<.001
UE	105 (13.7)	124 (11.9)	.243
LE (+buttock, groin)	107 (14.0)	195 (18.7)	.008
Chest	88 (11.5)	97 (9.29)	.125
Back (+flank)	306 (40.0)	463 (44.4)	.065
Abdomen	87 (11.4)	113 (10.8)	.713
Hand/foot	25 (3.27)	38 (3.64)	.670
Punch biopsy, n (%)	176 (23.0)	203 (19.4)	.066
Shave removal, n (%)	571 (74.6)	746 (71.5)	.133
Excision, n (%)	17 (2.22)	94 (9.00)	<.001
Other, n (%)	1 (0.130)	1 (0.100)	.243
Type of nevus, n (%):			
Compound	633 (82.8)	702 (67.2)	<.001
Junctional	124 (16.2)	342 (32.8)	<.001
Dermal	5 (0.650)	0 (0)	.009
NR	3 (0.390)	0 (0)	.043
Degree of dysplasia, n (%):			
Mild	188 (24.6)	405 (38.8)	<.001
Mild to moderate	174 (22.8)	255 (24.4)	.407
Moderate	403 (52.7)	414 (39.7)	<.001
Congenital features	96 (12.6)	37 (3.54)	<.001

LE, Lower extremity; *MM*, malignant melanoma; *NR*, not recorded; *UE*, upper extremity.

biopsy were more prevalent in the residual atypical nevus group (P = .09) whereas junctional nevi were more prevalent in the dermal scar only group (P = .003). There were no notable differences in patient demographics, lesion size, degree of dysplasia, or re-excisional margins between the 2 groups ($P > .05$). Among the specimens with residual atypical nevus (n = 90), 90% of the re-excisional specimens showed no clinically significant change in diagnosis, 7.72% of lesions were read as having no residual atypical melanocytic proliferation present, and 2.22% were upgraded to severely dysplastic.

The biopsy and re-excisional specimens of 2 upgraded lesions along with 18 randomly selected lesions in the melanocytic residuum group were reviewed by a blinded dermatopathologist (M. P. H.). The review of the 18 randomly selected lesions revealed no clinically significant change in diagnosis of both the biopsy specimen and re-excision. In the first upgraded lesion, the diagnosis during biopsy was changed to severely DN, and the reviewer agreed on the diagnosis of the re-excisional specimen as severely dysplastic. In the second upgraded lesion, the reviewer agreed that the biopsy specimen represented a moderately DN, and unfortunately, the slides of the re-excisional pathology were missing. Thus, after re-review of the original pathology, re-excision altered the clinical diagnosis in only 1 patient (0.2%).

DISCUSSION

The current management of mildly and moderately DN uses health care resources and yet, because of a lack of conclusive evidence in the dermatology literature, there are no agreed-upon clinical recommendations for the management of these lesions. In 1992, the National Institutes of Health Consensus Conference recommended that 0.2- to 0.5-cm margins should be taken when DN re-excision is indicated; however, in this publication, mildly-severely DN were grouped as 1 entity, and dermatologists and dermatopathologists were encouraged to develop their own schema for the diagnosis and management of DN.[14] Given the lack of further updates in clinical guidelines over the past few decades, standard practice varies significantly among clinicians.[7,8] In the current study, 64.7% of all mildly and moderately DN with positive surgical margins were subsequently re-excised, a percentage

Table II. Characteristics of re-excised margin-positive mildly and moderately dysplastic nevi

	Excision specimen with residual melanocytes, N = 90 (18.2%)	Excision specimen with residual scar, N = 405 (81.8%)	*P* value
Male, n (%)	34 (37.8)	154 (38.0)	.965
Mean age, y	39.5	42.5	.065
History of MM, n (%)	13 (14.4)	40 (9.88)	.205
Mean lesion size, mm	5.36	5.34	.933
Punch biopsy, n (%)	24 (26.7)	99 (24.4)	.659
Shave, n (%)	65 (72.2)	298 (73.6)	.792
Excision, n (%)	1 (1.11)	8 (1.98)	.579
Type of nevus, n (%):			
Compound	85 (94.4)	339 (83.7)	.009
Junctional	3 (3.33)	60 (14.8)	.003
Dermal	2 (2.22)	3 (0.740)	.204
NR	0 (0.00)	3 (0.74)	.413
Degree of dysplasia, n (%):			
Mild	3 (3.33)	13 (3.21)	.952
Mild to moderate	30 (33.3)	107 (26.4)	.185
Moderate	57 (63.3)	285 (70.4)	.191
Congenital features, n (%)	10 (11.1)	45 (11.1)	1.00
Re-excision margins mean, mm	2.65	2.75	.160

that is similar to what has previously been reported in the literature.[8,9]

General risk factors and variables may influence the decision to recommend re-excision. Patient demographics and history of melanoma were equally distributed among the group of lesions that were re-excised and those that were clinically monitored. Variables that appeared to influence the decision to re-excise include lesion size and degree of melanocytic dysplasia. Nevi were more likely to be re-excised if they were larger ($P < .001$) and as the degree of atypia increased from mildly to moderately dysplastic ($P < .001$). The latter association is also supported in a study by Reddy et al[9] that demonstrated that re-excision was more common as the degree of atypia increased ($P < .001$). It has recently been suggested that standardizing margin comments in the pathology reports of DN may reduce re-excision rates[15]; however, commenting on margin involvement is standard practice at our institution and likely did not significantly influence the results. Although no additional risk factors appear to statistically vary between the 2 groups, given the retrospective nature of this study, it is impossible to discern all of the factors that influenced clinical decision-making.

Given that the decision to re-excise is heavily dependent on the degree of histopathological atypia, clinical decision-making is further complicated by the lack of standardized objective histopathological criteria for the classification of DN atypia. Because of the significant heterogeneity that exists within DN, there are currently 4 separate accepted classification criteria for the grading of atypia.[4,13,16-18] Multiple studies have also demonstrated that both interpathologist and intrapathologist concordance for grading of DN atypia is poor.[16,19,20] Although increasing dermatopathology experience may improve reproducibility,[16] concordances rates range from 16% to 65%.[19] Therefore, the clinical decision to re-excise a mildly or moderately DN is ultimately based both on uncertain biological behavior in addition to subjective and variable grading criteria.

In view of the fact that that nearly 82% of mildly and moderately DN with positive surgical margins showed dermal scar only during re-excision, our results suggest that re-excising these lesions for the purpose of lesional clearance may not be warranted. Similar studies examining the surgical outcome of DN have previously been performed and estimated that only 14% to 33% of re-excised margin-positive DN will contain residual atypical nevus.[9-12] All of these studies were substantially smaller in size and included severely DN in addition to mildly and moderately DN in their analysis.[9-12]

It is unclear why the vast majority of re-excised specimens do not contain residual atypical nevus. Examination of the re-excisional specimen is limited by the number of sections taken during histopathological processing. Therefore, the entire specimen is often not fully examined in routine clinical practice, and this standard of care may result in the inability to appreciate small foci of residual melanocytes. In addition, some of specimens may contain atypical melanocytes that are close to the surgical margin but do not involve the true margin. Finally, inflammation

of the skin during biopsy and subsequent healing may result in immune-mediated destruction of residual melanocytes. Although the aforementioned explanations are speculative, these studies confirm that the histopathological yield from re-excising margin-positive mildly and moderately DN is low, and the benefit of ensuring complete nevus clearance may not offset the potential risk to the patient and cost associated with an additional procedure.

In addition to demonstrating a low histopathological yield during re-excision, the results of this study also show that there was no clinically significant alteration in diagnosis in 99.6% of cases before re-review and 99.8% of cases after re-review. More importantly, melanoma was not diagnosed in any of the 495 re-excisional specimens. It is possible that the alteration in diagnosis of the first re-reviewed biopsy specimen from moderately dysplastic to severely dysplastic is a reflection of trend that has occurred over the past few decades that favors upgrading the severity of melanocytic lesions.[20] However, given the fact that the dermatopathologist was blinded, there was no change in diagnosis in the 18 randomly selected lesions, and the re-review was less than 5 years after the initial diagnosis, we believe that the change of diagnosis from moderately dysplastic to severely dysplastic accurately reflects the features of this lesion. This extremely low rate of alteration in clinical diagnosis during re-excision has also been supported in the literature,[9,10,21] and melanoma found in the re-excisional specimen has been only associated with moderately to severely or severely DN rather than mildly and moderately DN.[9,10]

Minimizing cost while maintaining quality of care is central to health care reform. While examining biopsy techniques, the results of this study demonstrated that there was no statistically significant difference when comparing shave removal versus punch biopsy specimen. If a suture is placed, punch biopsy is a more costly procedure given the fact that patients must return to clinic for removal. Given the results of this study, we propose the use of shave removal of more than 1-mm thickness for the evaluation of clinically atypical nevi that are concerning for melanoma with the intent to remove the entire lesion. Finally, 91% of re-excisions in this study were performed via simple excision with layered closure. Given that procedures may be both costly and labor-intensive the financial implications associated with re-excision should be considered in clinical decision-making.

The main limitation of this study is the inability to assess the biological behavior of DN and specific risk for malignant transformation, particularly given the limited follow-up in this study. Unfortunately, it is challenging to design a study that would adequately address this issue, particularly given the number of patients needed to adequately power the results.[22] Hocker et al[23] conducted a prospective study of 115 patients in which margin-positive DN were clinically monitored rather than re-excised.[23] Patients were followed up for a mean of 17.4 years, and the authors reported that no malignant transformation occurred within these lesions. This phenomenon has also been reported in smaller studies with more limited follow-up.[24] It has been estimated that the risk of malignant transformation of single DN is approximately 1:10,000.[22] This relatively low rate of transformation multiplied by likelihood of yielding residual melanocytes during re-excision may support clinical monitoring alone.

Guidelines surrounding the management of DN are multifaceted and controversial. As such, a biopsy should be reserved for clinically atypical lesions concerning for melanoma rather than for the purpose of ruling out dysplasia alone. The results of this study suggest that the re-excisional yield of margin-positive mildly and moderately DN is low, and re-excision will not alter the clinical diagnosis in the vast majority of cases. Therefore, clinical monitoring rather than re-excision should be considered by clinicians. Additional long-term studies are warranted to further evaluate the biological potential of DN and assess the role of clinical monitoring and its effect on both malignant transformation and overall morbidity and mortality.

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