Melanoma and melanoma in-situ diagnosis after excision of atypical intraepidermal melanocytic proliferation: A retrospective cross-sectional analysis

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Background: There is little evidence to guide surgical management of biopsies yielding the histologic descriptor atypical intraepidermal melanocytic proliferation (AIMP).

Objective: Determine frequency of and factors associated with melanoma and melanoma in-situ (MIS) diagnoses after excision of AIMP and evaluate margins used to completely excise AIMP.

Methods: Retrospective, cross-sectional study of 1127 biopsies reported as AIMP and subsequently excised within one academic institution.

Results: Melanoma (in situ, stage 1A) was diagnosed after excision in 8.2% (92/1127) of AIMP samples. Characteristics associated with melanoma/MIS diagnosis included age 60-79 years (odds ratio [OR] 8.1, 95% confidence interval [CI] 2.5-26.2), age ≥80 years (OR 7.2, 95% CI 1.7-31.5), head/neck location (OR 4.9, 95% CI 3.1-7.7), clinical lesion partially biopsied (OR 11.0, 95% CI 6.7-18.1), and lesion extending to deep biopsy margin (OR 15.1, 95% CI 1.7-136.0). Average ± standard deviation surgical margin used to excise AIMP lesions was 4.5 ± 1.8 mm.

Limitations: Single-site, retrospective, observational study; interobserver variability across dermatopathologists.

Conclusion: Dermatologists and pathologists can endeavor to avoid ambiguous melanocytic designations whenever possible through excisional biopsy technique, interdisciplinary communication, and ancillary studies. In the event of AIMP biopsy, physicians should consider the term a histologic description rather than a diagnosis, and, during surgical planning, use clinicopathologic correlation while bearing in mind factors that might predict true melanoma/MIS. (J Am Acad Dermatol 2019;80:1403-9.)

Key words: ambiguous melanocytic lesions; atypical intraepidermal melanocytic proliferation; atypical junctional melanocytic hyperplasia; atypical junctional melanocytic proliferation; atypical melanocytic proliferation; biopsy; excision; lentiginous junctional melanocytic proliferation; melanoma; melanoma in situ.

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Melanocytic proliferations lie along a continuum of increasing histologic atypia from benign to malignant. Within this spectrum exists a subset of lesions that is intrinsically difficult to classify. Atypical intraepidermal melanocytic proliferation (AIMP) is a descriptive histopathologic term commonly used in these cases to denote morphology sharing some features with melanoma but failing to meet criteria of a definitive benign or malignant diagnosis.[1] Given the ambiguous malignant potential of these lesions and the possibility of remaining subclinical melanoma or melanoma in situ (MIS), a biopsy report describing AIMP warrants consideration for formal surgical excision with margins outside the biopsy site and any remaining pigmented lesion.

We aim to elucidate AIMP ontology and to add data to a growing body of dermatologic and dermatopathologic literature describing surgical outcomes of ambiguous melanocytic lesions.[2-4] We report the percentage of AIMP biopsies with postexcision melanoma and MIS diagnoses, describe clinical and histopathologic biopsy characteristics associated with this outcome, and evaluate the margins used for complete AIMP excision. This data will aid in patient counseling and surgical planning for AIMP.

CAPSULE SUMMARY

- Factors associated with malignancy diagnosis after excision of atypical intraepidermal melanocytic proliferation include incomplete sampling (lateral/deep margin), head or neck location, and age ≥60 years.
- Ambiguous melanocytic biopsy designations should be avoided, but, when present, warrant clinicopathologic correlation, with malignancy risk factors prompting consideration to excise as melanoma in situ.

METHODS

Experimental design

The Memorial Sloan-Kettering Cancer Center institutional review board approved this analysis. A text search of surgical pathology reports (January 1992-July 2016) using AIMP and synonyms included "atypical junctional melanocytic proliferation/hyperplasia," "atypical melanocytic proliferation," "lentiginous junctional melanocytic proliferation," and "proliferation of solitary units of melanocytes at the dermoepidermal junction." Inclusion criteria were biopsied lesions with slides described using the aforementioned search terms by in-house pathologists and subsequently excised at our institution.

Excluded biopsies were those reported to most likely represent melanoma/MIS, given the assumption that our dermatologists would interpret and subsequently treat this description as true malignancy. Conversely, AIMP reported unlikely to be melanoma/MIS were included, assuming that our dermatologists would not approach these as definitively benign entities.

Data collection

Data abstracted from biopsy reports included date, patient age, biopsy type, and gross specimen dimensions. Pathology report text was assessed for term used (AIMP or synonyms listed above), presence of pagetoid spread, description of a second surrounding or colliding histopathologic component (ie, nevus, carcinoma), positive margin presence and location, and special studies (immunohistochemical stains, molecular studies). The pathologist's description was ranked by degree of diagnostic uncertainty: (1) unlikely melanoma/MIS or melanoma/MIS not mentioned, (2) cannot exclude melanoma/MIS, and (3) melanoma/MIS listed in the differential diagnosis.

Prebiopsy clinical lesion size, personal melanoma/MIS history, and any local treatment before biopsy were recorded from the medical record. Clinical, operative, and pathology reports corresponding to each biopsy's subsequent excision were assessed for residual pigment presence/absence, treating specialty, surgical treatment type, treatment date, days between biopsy and treatment, margins of clinically normal-appearing tissue removed around the biopsied lesion, and final histopathologic description/diagnosis. When serial excisions (multiple standard excisions or staged-excision technique with delayed reconstruction) were required to attain negative histopathologic margins, total number of excisions was recorded with margins summed to yield a total margin used to clear.

Fig 1 details the algorithm used to determine whether biopsies represented full or partial samples of the clinically apparent pigment of their original lesions. The excision note was first examined for commentary about residual pigment at the previously biopsied site. If no such notation was found, the original biopsy note from clinic was assessed

Abbreviations used:

AIMP: atypical intraepidermal melanocytic proliferation
CI: confidence interval
MIS: melanoma in situ
OR: odds ratio

for biopsy type. If there was no record of an intentional excisional biopsy, gross specimen size was compared with clinical lesion size as a tertiary assessment.

Data analysis

Descriptive statistics and graphical methods were used to describe patient characteristics, lesions, surgical procedures, and histologic lesion evaluations. Descriptive and relative frequencies and 95% exact binomial confidence intervals (CIs) were used to present melanoma/MIS diagnosis burden. Logistic regression was used to present association between postexcision melanoma/MIS diagnosis and patient/lesion characteristics. All analyses were performed with Stata version 14.2 (Stata Corporation, College Station, TX).

RESULTS

Our database search yielded 1898 potential AIMP biopsies subsequently excised in-house. After excluding samples deemed most likely melanoma/MIS, 1127 biopsies remained for inclusion. Clinical and histopathologic characteristics are recorded in Table I and Table II, respectively.

Of 1127 AIMP biopsies, 515 were performed at outside institutions with slides subsequently reviewed and labeled AIMP by our pathologists. Of the remaining 612 biopsies performed in-house, 296 (48%) received adjunctive dermatopathologic studies in addition to hematoxylin-eosin staining before biopsy reporting. The institution's three dermatopathologists at time of data collection read 85.4% of biopsies and excisions.

The 2 cases ultimately treated with amputation were both AIMP reported in nail units, one of which yielded a postamputation diagnosis of MMIS.

Melanoma/MIS diagnosis after excision and surgical margins

Of 1127 biopsies interpreted as AIMP, 92 (8.2%, 95% CI 6.6-9.9%) were diagnosed as MIS (86/92) or invasive melanoma (6/92, ranging 0.2-0.6 mm) after excision. Excluding samples yielding scar on excision, 21% (92/442) were diagnosed as melanoma/MIS. Factors associated with melanoma/MIS diagnosis are outlined in Table III. Characteristics with greatest odds of melanoma/MIS diagnosis were age 60-79 years (odds ratio [OR] 8.1, 95% CI 2.5-26.2), age ≥80 years (OR 7.2, 95% CI 1.7-31.5), head or neck location (OR 4.9, 95% CI 3.1-7.7), partial biopsy of visible clinical lesion (OR 11.0, 95% CI 6.7-18.1), and deep biopsy margin involvement (OR 15.1, 95% CI 1.7-136.0). Male sex, prior local treatment, and melanoma/MIS noted in differential diagnosis yielded statistically significant but smaller odds ratios.

After controlling for partial biopsy, all melanoma/MIS-associated characteristics remained significant (male sex, OR 2.0, 95% CI 1.3-3.2; age 60-79 years, OR 9.0, 95% CI 2.7-30.0; age ≥80 years, 95% CI 1.8-38.3; head or neck location, OR 3.4, 95% CI 2.1-5.6; melanoma/MIS in differential diagnosis, OR 4.0, 95% CI 2.3-7.0; positive deep margin, OR 18.3, 95% CI 1.9-172.6), except for history of prior treatment, which lost significance (OR 1.4, 95% CI 0.6-3.2).

Average ± standard deviation surgical margin used to excise AIMP lesions was 4.5 ± 1.8 mm, with 94.9% (1070/1127) requiring 1 excision. Positive or equivocal margins led to serial excisions in 5.1% (57/1127) of cases. For the 86 samples ultimately diagnosed as MIS, average ± standard deviation surgical margin was 6.5 ± 2.4 mm; for the 6 invasive melanomas, 10.4 ± 5.6 mm.

DISCUSSION

Central to this study is identification of partial biopsies, here defined as those failing to capture all visible pigment from their source lesions. These showed odds of melanoma/MIS 11 times those of full biopsies: intentional excisional biopsies and punch/shave biopsies of all visible pigment. Although the American Academy of Dermatology and National Comprehensive Cancer Network recommend narrow excisional biopsies encompassing the clinically apparent breadth of suspicious melanocytic lesions,[5,6] a desire to spare tissue in cosmetically and/or functionally sensitive areas might prompt a decision to partially sample a lesion, inevitably increasing risk for sampling error. Ultimately, complete sampling of suspicious pigmented lesions—providing dermatopathologists with maximum pathologic diagnostic information—is likely to be in the patient's best interest. Cases potentially inappropriate for complete excisional biopsy, such as broad lesions with suspected horizontal spread near vital anatomy, might benefit from multiple scouting biopsies to optimize diagnostic accuracy.

An average 4.5-mm margin was used to clear AIMP lesions, aligning with the lower bound of National Comprehensive Cancer Network's 5—10-mm

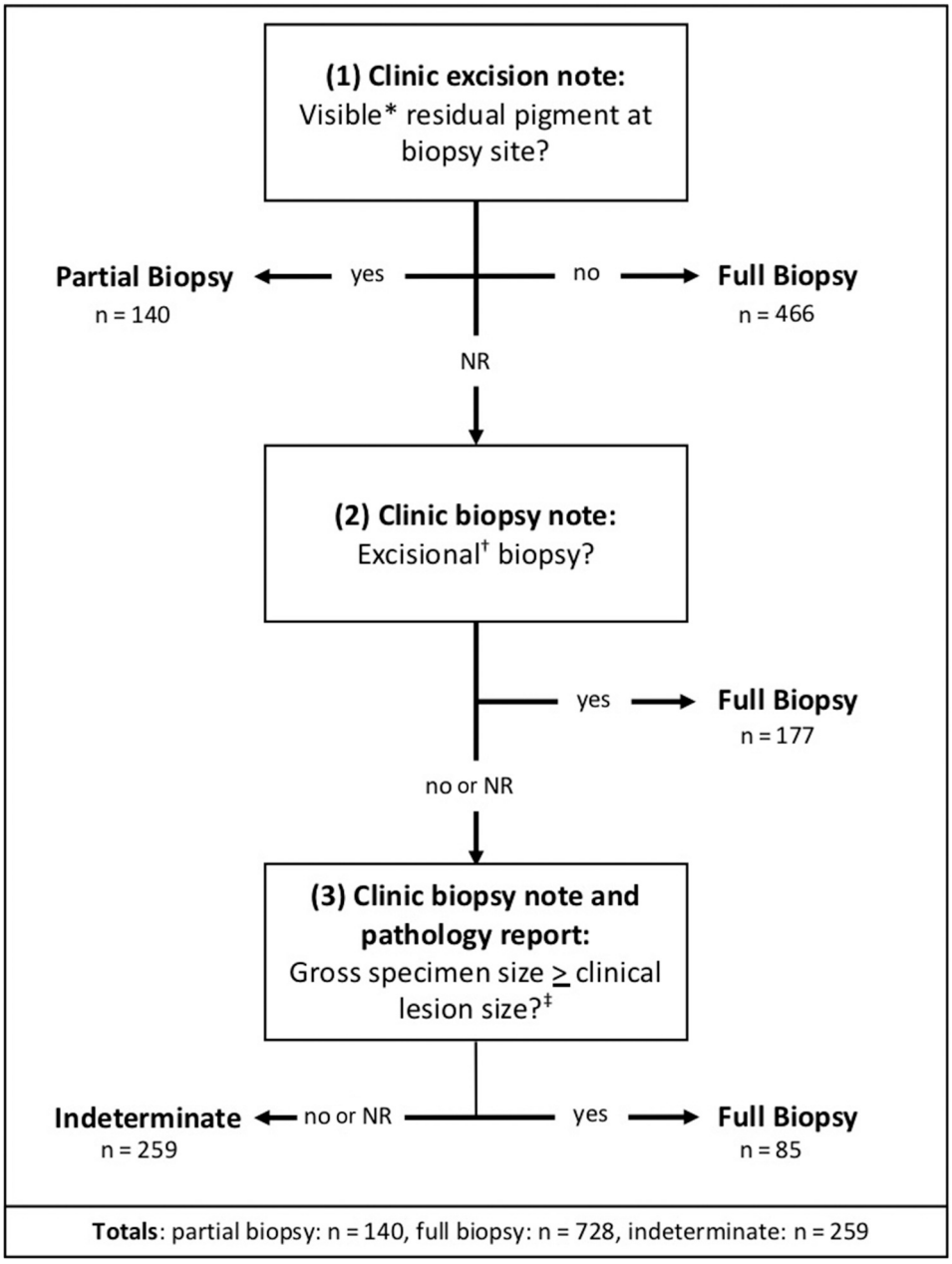

Fig 1. Algorithm to determine full versus partial biopsy for 1127 AIMP Lesions. NR, not recorded. *Including Woods Lamp examination. †Including shave removal, shave excision, punch removal, punch excision, saucerization. ‡Assumes shrinkage of gross tissue.

recommendation for MIS wide excision.[7] Those AIMP ultimately diagnosed MIS, however, yielded an average 6.5-mm surgical margin for histologic clearance, possibly due to re-excisions carried out after MIS diagnosis. This further underscores the utility of full pigmented lesion biopsies, which might reduce likelihood of ambiguous biopsy descriptions leading to re-excisions.

Our study revealed nearly all characteristics associated with melanoma/MIS diagnosis to remain significant after controlling for partial biopsy, diverging from a recent analysis of head or neck, hand, and foot AIMP biopsies in which partial biopsy was the only clinicopathologic factor associated with post-excision melanoma/MIS.[4] These other clinical characteristics might, thus, remain useful to prognosticate

Table I. Clinical characteristics of sample

Clinical variables	Value*
Age at biopsy, y, mean (SD) [range]	56.4 (15.2) [7-93]
Sex	
Female	658 (58.3)
Male	469 (41.6)
Anatomic location	
Head or neck	192 (17.0)
Trunk or extremity	827 (73.4)
Hand or foot	86 (7.6)
Nail	13 (1.2)
Genitalia	9 (0.8)
Lesion diameter, mm, mean (SD) [range]†	6.6 (5.6) [1-50]
Melanoma/MIS history	
Yes	440 (39.0)
No	676 (60.0)
Not recorded	11 (1.0)
Prior treatment for lesion	
Yes (laser, biopsy, excision, not specified)	60 (5.3)
No	1056 (93.7)
Not recorded	11 (1.0)
Treating specialty	
Dermatology	909 (80.7)
Surgical oncology	188 (16.7)
Other (head or neck surgery, plastic surgery, hand surgery, gyneco-logic surgery)	30 (2.7)
Follow-up treatment	
Excision	1062 (94.2)
Shave excision	47 (4.2)
Punch excision	16 (1.4)
Amputation	2 (0.2)
Time between biopsy and treatment, days, average (SD) [range]‡	69 (45) [3-2214]
AIMP re-excision diagnosis	
Melanoma	6 (0.5)
Melanoma in situ	86 (7.6)
Atypical melanocytic lesion§	266 (23.6)
Atypical or dysplastic nevus	37 (3.3)
Benign nevus	23 (2.0)
Other, benign	24 (2.1)
Scar	685 (60.8)
Margin used to clear, mm, average (SD) [range]‖	4.5 (1.8) [1-19]
Serial excisions needed	
No	1070 (94.9)
Yes, 2	53 (4.7)
Yes, 3	4 (0.4)

SD, Standard deviation.
*Values are N (%) except where indicated.
†Data available for 505 samples.
‡Data available for 1121 samples.
§Composite category of atypical melanocytic diagnoses and descriptors, such as atypical intraepidermal melanocytic proliferation, atypical junctional melanocytic hyperplasia, and melanocytic hyperplasia.
‖Data available for 945 excisions.

Table II. Histopathologic characteristics of sample biopsies

Clinical variable	N (%)
Biopsy type	
Shave	702 (62.3)
Punch	66 (5.9)
Excisional biopsy	247 (21.9)
Nail biopsy	12 (1.1)
Not recorded	100 (8.9)
Full vs partial biopsy	
Full	728 (64.6)
Partial	140 (12.4)
Indeterminate	259 (23.0)
Term used to describe pathology	
Atypical intraepidermal melanocytic proliferation	728 (64.6)
Lentiginous/junctional melanocytic proliferation	328 (29.1)
Atypical melanocytic proliferation	71 (6.3)
Degree of melanoma/MIS uncertainty	
Least likely melanoma/MIS or does not mention melanoma	501 (44.5)
Cannot exclude melanoma/MIS	248 (22.0)
Melanoma/MIS in differential	378 (33.5)
Pagetoid spread	
Yes	266 (23.6)
No	861 (76.4)
Collision lesion	
With a nevus or other melanocytic lesion	289 (25.6)
With a nonmelanocytic lesion	85 (7.5)
No collision reported	753 (66.8)
Margins involved in biopsy specimen	
Lateral	334 (29.6)
Deep or deep and lateral	31 (2.8)
Unspecified positive margin	274 (24.3)
Negative margin explicitly noted	80 (7.1)
Not recorded	408 (36.2)
Special stains performed in-house*	
Yes	296 (48.3)
Not recorded	316 (51.6)

*612 biopsies performed in-house, 515 biopsies performed at outside institutions.

greater or lower melanoma/MIS odds even for full lesion biopsies.

Our study's total melanoma/MIS rate is higher than that of a prior study, which reported 4.2% melanoma/MIS among 306 AIMP biopsies,[2] likely secondary to our cancer center–derived study population. The analyses reveal similar melanoma/MIS-associated characteristic profiles, notably head or neck location, positive deep margin, and melanoma/MIS in initial biopsy differential.[2] Diverging from the prior study, we report neither hand or foot location nor punch biopsy technique to associate with melanoma/MIS diagnosis.[2] The significance of this

Table III. Clinical and histopathologic variables associated with melanoma/MIS diagnosis after excision of AIMP

		Melanoma/MIS diagnosis after excision		
Characteristic	**Total, n (%)**	**No, n (%)**	**Yes, n (%)**	**OR (95% CI)**
Sex				
Female	658 (58.4)	619 (59.8)	39 (42.4)	1.0 (Referent)
Male	469 (41.6)	416 (40.2)	53 (57.6)	2.0 (1.3-3.1)
Age, y				
<40	172 (15.3)	169 (16.4)	3 (3.3)	1.0 (Referent)
40-59	428 (38.2)	404 (39.3)	24 (26.1)	3.3 (1.0-11.3)
60-79	477 (42.6)	417 (40.5)	60 (65.2)	8.1 (2.5-26.2)
≥80	44 (3.9)	39 (3.8)	5 (5.4)	7.2 (1.7-31.5)
Anatomic location				
Trunk or extremity	827 (73.4)	782 (75.6)	45 (48.9)	1.0 (Referent)
Head or neck	192 (17)	150 (14.5)	42 (45.7)	4.9 (3.1-7.7)
Hand or foot	86 (7.6)	85 (8.2)	1 (1.1)	0.2 (0.0-1.5)
Other (nail or genitals)	22 (2.0)	18 (1.7)	3 (4.3)	2.9 (0.8-10.2)
Melanoma/MIS history				
No	676 (60.6)	629 (61.4)	47 (51.1)	1.0 (Referent)
Yes	440 (39.4)	395 (38.6)	45 (48.9)	1.5 (1.0-2.3)
Prior treatment for lesion				
No	1056 (94.6)	974 (95.1)	82 (89.1)	1.0 (Referent)
Yes	60 (5.4)	50 (4.9)	10 (10.9)	2.4 (1.2-4.9)
Biopsy type				
Shave	702 (68.3)	638 (67.4)	64 (79.0)	1.0 (Referent)
Punch	66 (6.4)	56 (5.9)	10 (12.4)	1.8 (0.9-3.7)
Excision	247 (24.1)	242 (25.6)	5 (6.2)	0.2 (0.1-0.5)
Nail	12 (1.2)	10 (1.1)	2 (2.5)	2.0 (0.4-9.3)
Biopsy				
Full	728 (64.6)	696 (67.3)	32 (34.8)	1.0 (Referent)
Partial	140 (12.4)	93 (9)	47 (51.1)	11.0 (6.7-18.1)
Indeterminate	259 (23)	246 (23.8)	13 (14.1)	1.1 (0.6-2.2)
Term used to describe pathology				
Atypical intraepidermal melanocytic proliferation	728 (64.6)	666 (64.4)	62 (67.4)	1.0 (Referent)
Lentiginous/junctional melanocytic proliferation	328 (29.1)	303 (29.3)	25 (27.2)	0.9 (0.5-1.4)
Atypical melanocytic proliferation	71 (6.3)	66 (6.4)	5 (5.4)	0.8 (0.3-2.1)
Degree of melanoma/MIS uncertainty				
Least likely, does not mention	501 (44.5)	481 (46.5)	20 (21.7)	1.0 (Referent)
Cannot exclude	248 (22)	230 (22.2)	18 (19.6)	1.9 (1.0-3.6)
In differential	378 (33.5)	324 (31.3)	54 (58.7)	2.0 (1.5-2.6)
Pagetoid spread				
No	861 (76.4)	786 (75.9)	75 (81.5)	1.0 (Referent)
Yes	266 (23.6)	249 (24.1)	17 (18.5)	0.7 (0.4-1.2)
Collision lesion				
No collision reported	753 (66.8)	690 (66.7)	63 (68.5)	1.0 (Referent)
With a nevus, other melanocytic lesion	289 (25.6)	264 (25.5)	25 (27.2)	1.0 (0.6-1.7)
With a nonmelanocytic lesion	85 (7.5)	81 (7.8)	4 (4.4)	0.5 (0.2-1.5)
Margins involved in biopsy specimen				
Negative margin explicitly noted	80 (7.1)	79 (10.1)	1 (1.1)	1.0 (Referent)
Lateral	334 (29.6)	306 (39.0)	28 (30.4)	7.2 (1.0-53.9)
Deep, deep and lateral	31 (2.8)	26 (3.3)	5 (5.4)	15.1 (1.7-136.0)
Unspecified positive margin	274 (24.3)	250 (31.8)	24 (26.1)	7.6 (1.0-57.0)
Not recorded	408 (36.2)	374 (47.6)	34 (37.0)	7.2 (1.0-53.2)
Special stains performed in-house*				
No	316 (51.6)	288 (51.1)	28 (58.3)	1.0 (Referent)
Yes	296 (48.3)	276 (48.9)	20 (41.7)	0.7 (0.4-1.4)

CI, Confidence interval; *MIS*, melanoma in situ; *OR*, odds ratio.

*515 biopsies performed at outside institution; 612 biopsies performed in-house.

is unclear and might reflect differing institutional sampling practices and pathology reporting.

There is interobserver variability inherently associated with a subjective histopathologic descriptor such as AIMP. That we do not explicitly account for this variability is a limitation of our study. Other limitations include the study's retrospective nature and restriction to 1 academic cancer center subject to referral bias.

CONCLUSION

The intrinsic diagnostic uncertainty of biopsies reported as AIMP presents a therapeutic dilemma. Factors associated with postexcision melanoma/MIS diagnosis, particularly incomplete clinical pigment sampling, deep biopsy margin involvement, and age ≥60 years, should prompt consideration to excise with surgical margins in line with MIS guidelines. In carefully selected clinical settings, complete biopsies with few risk factors might lead the clinician not to intervene further.

Although AIMP and other similar descriptors might periodically be unavoidable, further steps can and should be taken to minimize ambiguity in melanocytic biopsies. Complete excisional biopsies of suspicious pigmented lesions and clinical information sharing with pathologists (lesion size, appearance, and history; full vs partial biopsy) enhance clinicopathologic correlation. Noninvasive imaging such as dermoscopy and reflectance confocal microscopy aid in diagnosis and mapping before or after biopsy, particularly in cosmetically or functionally sensitive areas unfavorable for excisional biopsy.[8] Pathologists might also curtail ambiguous biopsy descriptions with ancillary diagnostic techniques. Immunohistochemistry, cytogenetics, and gene expression assays have shown potential in improving diagnostic precision, particularly in combination with clinical imaging approaches.[1] The conversation about AIMP must underscore effective interdisciplinary communication between dermatologist and pathologist to minimize ambiguity and optimize management of atypical melanocytic lesions.

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REFERENCES

1. Ensslin CJ, Hibler BP, Lee EH, Nehal KS, Busam KJ, Rossi AM. Atypical melanocytic proliferations: a review of the literature. *Dermatol Surg*. 2018;44(2):159-174.
2. Zhang J, Miller CJ, Sobanko JF, Shin TM, Etzkorn JR. Diagnostic change from atypical intraepidermal melanocytic proliferation to melanoma after conventional excision-a single academic institution cross-sectional study. *Dermatol Surg*. 2016;42(10):1147-1154.
3. Zhang J, Miller CJ, Sobanko JF, Shin TM, Etzkorn JR. Frequency of and factors associated with positive or equivocal margins in conventional excision of atypical intraepidermal melanocytic proliferations (AIMP): a single academic institution cross-sectional study. *J Am Acad Dermatol*. 2016;75(4):688-695.
4. Jew O, Miller CJ, Shin TM, Sobanko JF, Etzkorn JR. Diagnostic change from atypical intraepidermal melanocytic proliferation to melanoma is more likely when clinically visible residual pigment remains after biopsy. *Dermatol Surg*. 2018;44(7):1024-1026.
5. Coit DG, Andtbacka R, Bichakjian CK, et al. Melanoma. *J Natl Compr Canc Netw*. 2009;7(3):250-275.
6. Bichakjian CK, Halpern AC, Johnson TM, et al. Guidelines of care for the management of primary cutaneous melanoma. *J Am Acad Dermatol*. 2011;65(5):1032-1047.
7. Melanoma NCCN. *Clinical Practice Guidelines in Oncology (NCCN Guidelines) 2018; version 2*; 2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf. Accessed February 16, 2018.
8. Yelamos O, Cordova M, Blank N, et al. Correlation of handheld reflectance confocal microscopy with radial video mosaicing for margin mapping of lentigo maligna and lentigo maligna melanoma. *JAMA Dermatol*. 2017;153(12):1278-1284.