A retrospective cohort study of the diagnostic value of different subtypes of atypical pigment network on dermoscopy

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Background: Atypical network encompasses several patterns. Few studies assess the sensitivity, specificity, and positive and negative predictive values of network subtypes.

Objective: We assessed the diagnostic value of atypical network subtypes and their histopathologic correlates in cutaneous melanocytic lesions.

Methods: A retrospective search (2014-2018) from a high-risk melanoma clinic for cases scored for atypical network with accompanying dermoscopic photographs yielded 120 lesions (15 melanoma; 30 severely, 38 moderately, and 32 mildly atypical nevi; 4 compound nevi; and 1 junctional nevus). A dermatopathologist blinded to diagnosis assessed dermoscopic and histologic features. Network abnormality correlates with histopathology and clinical diagnoses were assessed with sensitivity, specificity, positive and negative predictive values, and odds ratios.

Results: A multivariable model with shiny white streaks (odds ratio 3.02) and inverse network (OR 4.46) was most predictive of melanoma or severe atypia. Positive predictive value for melanoma or severe atypia in decreasing order was inverse network (73.9%), shiny white streaks (71.4%), loss of network (46%), branched streaks (29.4%), and thick brown lines (28.4%).

Limitations: Cases were retrospectively found from a pigmented lesion clinic and evaluated by a single dermatopathologist.

Conclusion: Shiny white streaks and inverse network are most predictive of melanoma or severe atypia and warrant biopsy if found on dermoscopy. (J Am Acad Dermatol 2020;83:1028-34.)

Key words: atypical; atypical network; branched streaks; dermis; dermoscopy; epidermis; fibroplasia; inverse network; lentiginous; loss of network; melanoma; nevi; pigment; rete; shiny white streaks; thick brown lines.

INTRODUCTION

The presence of an atypical pigment network on dermoscopic examination of cutaneous melanocytic neoplasms has a reported specificity for melanoma ranging from 53.6% to 95.2%,[1-9] which is not surprising because an atypical network can be variably

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defined. Some definitions include various combinations of thickened brown lines, black or gray lines, rhomboidal structures, branched streaks, angulated lines, loss of network, inverse network, and regression features such as shiny white streaks. Although the presence of an atypical pigment network increases the likelihood of a melanoma diagnosis, it may also be present in a significant number of benign cutaneous melanocytic lesions, and there is considerable variability when it comes to defining an atypical network even among expert dermoscopists.[10]

Because the definition of atypical pigment network is broad, it is expected that there will be low interobserver agreement regarding its presence.[11] In a study determining the accuracy of dermoscopic features for diagnosis, the interobserver agreement for atypical network was estimated to be approximately 0.393, highlighting the variable interpretation of this feature.[2] Additionally, because the combination of features included as a network aberration in each atypical network study varies, it is difficult to know the specificity of given subpatterns of atypical network such as thick brown lines, gray lines, or branched streaks.

In this study, we aimed to study the sensitivity, specificity, positive predictive value, and negative predictive value of specific subpatterns of atypical network. We included thick brown lines, shiny white streaks, loss of network, inverse network, and branched streaks as distinct subpatterns of atypical network. We hope to demonstrate which network aberrations have the greatest utility in differentiating benign and malignant cutaneous melanocytic lesions and the morphologic correlate for each subpattern.

CAPSULE SUMMARY

- There are limited specificity and positive predictive value data for atypical network subtypes.
- Loss of network, thickened brown lines, and branched streaks had positive predictive values less than 20% for melanoma. Shiny white streaks and inverse network in a melanocytic lesion are most predictive for melanoma or severe atypias.

METHODS

Case selection

This was a retrospective cohort study. After institutional review board approval was obtained, our dermatopathology database was retrospectively searched from 2014 to 2018 for the term "score." Selected cases met the following criteria: the pathology requisition described an atypical network on dermoscopy and the clinician bisected or scored the area of network abnormality, and there were corresponding gross and nonpolarized and polarized dermoscopic photographs. One hundred twenty cases were included: 15 melanoma, 30 dysplastic nevi with severe atypia, 38 dysplastic nevi with moderate atypia, 32 dysplastic nevi with mild atypia, 4 compound nevi, and 1 junctional nevus.

Histologic and dermoscopic assessment

At diagnosis, the following dermoscopic features were assessed: thick brown lines, loss of network, branched streaks, inverse network, and shiny white streaks. The presence or absence of certain histologic features in each case was assessed by a board-certified dermatopathologist who was blinded to the diagnosis and dermoscopic features. The following histologic features were assessed: epidermal pigment, dermal pigment, increased fibroplasia, blunting of rete ridges, broadening of interretial spaces, expansile nests, pagetosis, extensive lentiginous growth, and fusion of rete ridges.

Statistical analysis

Cases were stratified in 2 ways: melanoma versus nonmelanoma, and melanoma and dysplastic nevi with severe atypia versus all other benign diagnoses. All histologic diagnoses were standard-of-care diagnoses from clinical care. Statistical comparisons were conducted with R (version 3.5.1) (The R Foundation, Vienna, Austria). For each dermoscopic feature, sensitivities, specificities, negative predictive values, and positive predictive values were calculated with contingency tables. Logistic regression was performed for univariable analysis of the association of each dermoscopic feature with melanoma or melanoma and dysplastic nevi with severe atypia, and for each dermoscopic feature with each histologic one. The MASS package glm (The R Foundation) function in R was used for univariable and multivariable logistic regression.[12] Dermoscopic features found to be statistically significant for a positive correlation with melanoma or severe atypia in univariable analysis were included in a stepwise logistic regression with backward selection for multivariable analysis. Statistical significance was set at $P < .05$ for all statistical comparisons except for the comparison of histologic features with dermoscopic features, which was set at $P < .006$,

Abbreviation used:

OR: odds ratio

adjusted with the Bonferroni correction for multiple comparisons.[13]

RESULTS

Clinical features

Our cohort comprised 57% women and 43% men, with an average age of 40.5 ± 11.6 years and a median of 37 years (range 24-71 years). All patients were white and 90% had Fitzpatrick skin type I to II. The remaining patients (12/120, 10%) had Fitzpatrick skin type III. The majority of the lesions were located on the trunk (85.8%), with the rest on the extremities (15 cases, 12.5%) and head and neck (2 cases, 1.7%). Of the 120 cases, the distribution consisted of 2 invasive melanomas (1.7%), 13 melanomas in situ (10.8%), 30 dysplastic nevi with severe atypia (25%), 32 dysplastic nevi with moderate atypia (26.7%), 38 dysplastic nevi with mild atypia (31.7%), 4 compound nevi (3.3%), and 1 junctional nevus (0.8%). Of the melanomas, 10 were superficial spreading, 1 was lentigo maligna type, and 4 did not have a histologic subtype labeled. The Breslow depth of the 2 invasive melanomas was 0.24 and 0.3 mm.

The overall frequency of each network abnormality was as follows: thick brown lines (74/120, 61.7%), loss of network (50/120, 41.7%), branched streaks (17/120, 14.2%), inverse network (23/120, 19.2%), and shiny white streaks (21/120, 17.5%). Among 15 melanoma cases, 8 had thick brown lines (8/15, 53.3%), 7 had loss of network (7/15, 46.7%), 7 had shiny white streaks (7/15, 46.7%), 5 had inverse network (5/15, 33.3%), and 3 had branched streaks (3/15, 20%). Of dysplastic nevi with severe atypia, 13 had thick brown lines (13/30, 43.3%), 16 had loss of network (16/30, 53.3%), 8 had shiny white streaks (8/30, 26.7%), 12 had inverse network (12/30, 40%), and 2 had branched streaks (2/30, 6.7%).

Eight melanomas had shiny white streaks or inverse network. Four of these 8 melanomas had both shiny white streaks and inverse network. Three cases had only shiny white streaks (3/8, 37.5%) and 1 case had only inverse network (1/8, 12.5%). In the combined cohort of melanoma and severely dysplastic nevus, 22 had shiny white streaks or an inverse network. Among these 22 cases, 10 (10/22, 45.5%) had both shiny white streaks and an inverse pigment network. Five cases had only shiny white streaks (5/22, 22.7%) and 7 had only an inverse network (7/22, 31.8%).

Sensitivity, specificity, negative predictive value, and positive predictive value

Among the different network aberrations, the specificity of the dermoscopic features for melanoma in decreasing order was shiny white streaks (86.7%) and branched streaks (86.7%), inverse network (82.9%), loss of network (59.1%), and thick brown lines (37.1%). The sensitivities in decreasing order were thick brown lines (53.3%), loss of network (46.7%) and shiny white streaks (46.7%), inverse network (33.3%), and branched streaks (20%). The negative predictive value in decreasing order was shiny white streaks (91.9%), inverse network (89.7%), loss of network (88.6%), branched streaks (88.4%), and thick brown lines (84.8%). The positive predictive value in decreasing order was shiny white streaks (33.3%), inverse network (21.7%), branched streaks (17.7%), loss of network (14%), and thick brown lines (10.8%). See Table I for details.

When melanoma and dysplastic nevi with severe atypia were grouped together, the specificity of the various atypical network dermoscopy features in decreasing order was as follows: shiny white streaks (92%) and inverse network (92%), branched streaks (84%), loss of network (64%), and thick brown lines (29.3%). The sensitivity of these features in decreasing order was loss of network (51.1%), thick brown lines (46.7%), inverse network (37.8%), shiny white streaks (33.3%), and branched streaks (11.1%). The negative predictive value in decreasing order was inverse network (71.1%), shiny white streaks (69.7%), loss of network (68.6%), branched streaks (61.2%), and thick brown lines (47.8%). The positive predictive value in decreasing order was inverse network (73.9%), shiny white streaks (71.4%), loss of network (46%), branched streaks (29.4%), and thick brown lines (28.4%). See Table I for details.

Univariable and multivariable analysis

Shiny white streaks were the only dermoscopic feature that was statistically significantly associated with melanoma (odds ratio [OR] 5.69; $P = .003$) and thus was the most predictive model for a diagnosis of melanoma. Although loss of network, branched streaks, and inverse network were all more common in the melanomas compared with the nevi, the difference did not reach statistical significance.

When comparing melanoma and dysplastic nevi with severe atypia with the remaining cases, inverse pigment network (OR 6.98; $P < .001$) and shiny white streaks (OR 5.75; $P < .001$) were statistically correlated with a diagnosis of melanoma or severe dysplasia. Although loss of network was more

Table I. Sensitivity, specificity, positive predictive value, negative predictive value, and odds ratio of dermoscopic features for melanoma and for melanoma plus dysplastic nevi with severe atypia versus all other benign lesions

Dermoscopic features	Sensitivity, %	Specificity, %	PPV, %	NPV, %	OR (95% CI)	*P* value
Melanoma						
Thick brown lines	53.3	37.1	10.8	84.8	0.68 (0.23–2.06)	.48
Loss of network	46.7	59.1	14.0	88.6	1.26 (0.41–3.77)	.68
Branched streaks	20.0	86.7	17.7	88.4	1.62 (0.34–5.93)	.49
Inverse network	33.3	82.9	21.7	89.7	2.42 (0.69–7.71)	.15
Shiny white streaks	46.7	86.7	33.3	91.9	5.69 (1.75–18.43)	.003*
Melanoma + severe atypia						
Thick brown lines	46.7	29.3	28.4	47.8	0.36 (0.17–0.78)	.009*
Loss of network	51.1	64.0	46.0	68.6	1.86 (0.88–3.97)	.11
Branched streaks	11.1	84.0	29.4	61.2	0.66 (0.20–1.92)	.46
Inverse network	37.8	92.0	73.9	71.1	6.98 (2.61–21.07)	<.001*
Shiny white streaks	33.3	92.0	71.4	69.7	5.75 (2.12–17.47)	<.001*

Logistic regression was used for univariable analysis, with statistical significance set at $P < .05$.
CI, Confidence interval; *NPV*, negative predictive value; *OR*, odds ratio; *PPV*, positive predictive value.
*Statistically significant.

common in the combined cohort of melanomas and severely dysplastic nevi than in the cohort consisting of conventional, mild, and moderately dysplastic nevi, this did not reach statistical significance (Table I). Stepwise logistic regression with backwards selection was performed with a starting model that consisted of the dermoscopic features found to be positively statistically significant in univariable analysis: inverse pigment network and shiny white streaks. A model consisting of inverse network (OR 4.46; 95% confidence interval 1.48-14.58; $P = .009$) and shiny white streaks (OR 3.02; 95% confidence interval 0.94-10.12; $P = .06$) was found to be most predictive of a diagnosis of melanoma or dysplastic nevus with severe atypia.

HISTOLOGIC CORRELATION WITH DERMOSCOPIC FEATURES

When the correlation between the dermoscopic and histologic features was examined, the following pairings were found to be statistically significant. Thick brown lines were strongly correlated with pigmented epidermis (OR 3.99; $P = .005$) and inversely correlated with rete blunting (OR 0.16; $P < .001$). Inverse network corresponded with increased fibroplasia (OR 5.34; $P = .001$) and expansile nests (OR 8.05; $P = .001$). Shiny white streaks were associated with increased fibroplasia (OR 16.60; $P < .001$) and broadening of the interretial space (OR 9.67; $P < .001$). Last, loss of network and branched streaks did not have a statistically significant association with any of the measured histologic features (Table II).

DISCUSSION

The presence of pigment aggregating around rete ridges creates the classic regular pigment network typical of many benign nevi. Atypical network has variable definitions, including thickened brown lines, black or gray lines, rhomboidal structures, branched streaks, angulated lines, loss of network, inverse network, and regression features such as shiny white streaks. Therefore, the range of different network aberrations possible in a lesion described as having an atypical pigment network is broad. This may be one of several reasons that the sensitivity and specificity reported for the presence of an atypical pigment network are highly variable, depending on the study.[1-9] In this study, we assessed the sensitivity, specificity, positive predictive value, and negative predictive value of some specific network aberrations including thickened brown lines, loss of network, inverse network, shiny white streaks, and branched streaks. Although some of the other network abnormalities described in the literature were also observed, such as gray lines, they were present at too small a frequency to allow statistical assessment.

The lesions included in this study were all from white patients with mostly Fitzpatrick I and II skin types assessed in a high-risk pigmented-lesion clinic. Therefore, the conclusions in the study may be most relevant to that population. Because many of these patients have a large number of dysplastic nevi, the number of nevi is likely to greatly outnumber the total number of melanomas for any given patient. Thus, it can be argued that the positive predictive value of the different network aberrations studied is

Table II. Univariable analysis with logistic regression comparing the association of each dermoscopic feature with each histologic one

	Dermoscopic features									
	Thick brown lines		Loss of network		Branched streaks		Inverse network		Shiny white streaks	
Histologic features	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Pigmented epidermis	3.99 (1.57–10.87)	.005*	0.47 (0.18–1.19)	.11	0.74 (0.23–2.83)	.62	0.26 (0.10–0.73)	.009	0.29 (0.10–0.84)	.02
Pigmented dermis	1.68 (0.79–3.65)	.18	0.35 (0.16–0.74)	.007	0.70 (0.23–2.00)	.52	0.53 (0.19–1.35)	.20	0.48 (0.16–1.29)	.16
Increased fibroplasia	0.36 (0.16–0.83)	.02	0.55 (0.22–1.26)	.17	0.55 (0.12–1.83)	.37	5.34 (2.05–14.37)	.001*	16.60 (5.65–56.99)	<.001*
Rete blunting	0.16 (0.07–0.37)	<.001*	2.88 (1.32–6.42)	.009	1.16 (0.37–3.32)	.79	1.80 (0.70–4.58)	.22	3.56 (1.36–9.65)	.01
Interrete broadening	0.68 (0.27–1.70)	.40	1.88 (0.77–4.72)	.17	0.49 (0.07–1.92)	.37	2.06 (0.70–5.66)	.17	9.67 (3.43–28.75)	<.001*
Expansile nests	0.27 (0.07–0.92)	.04	0.67 (0.17–2.28)	.54	1.24 (0.18–5.32)	.79	8.05 (2.30–30.31)	.001*	2.68 (0.66–9.56)	.14
Pagetosis	0.56 (0.21–1.49)	.24	1.91 (0.73–5.15)	.19	0.63 (0.09–2.50)	.56	2.83 (0.94–8.09)	.06	2.43 (0.76–7.15)	.12
Extensive lentiginous growth	0.79 (0.37–1.71)	.55	1.83 (0.86–3.94)	.12	0.71 (0.21–2.08)	.55	1.49 (0.58–3.76)	.40	2.92 (1.12–7.87)	.03
Rete fusion	1.40 (0.67–2.95)	.37	0.94 (0.46–1.96)	.88	0.48 (0.15–1.35)	.17	1.33 (0.53–3.39)	.55	0.86 (0.33–2.21)	.75

Statistical significance set at $P < .006$, adjusted with Bonferroni correction.
CI, Confidence interval; *OR,* odds ratio.
*Statistically significant.

most relevant. The positive predictive value for shiny white streaks and inverse pigment network for a diagnosis of melanoma was 33% and 22%, respectively. The respective positive predictive value of shiny white streaks and inverse pigment network for a diagnosis of melanoma or severely dysplastic nevus was 71% and 74%. Because there is overlap between severely dysplastic nevus and early radial growth phase melanoma and both of these are typically re-excised, it can be argued that the positive predictive value for the combined cohort of melanoma or severely dysplastic nevus is most relevant. These 2 aberrations have fairly high positive predictive value and suggest a biopsy should be performed even if present in the absence of any other dermoscopic aberrations in a melanocytic neoplasm. In a multivariable stepwise logistic regression with backwards selection, a model consisting of inverse network (OR 4.46; $P = .009$) and shiny white streaks (OR 3.02; $P = .06$) was found to be most predictive of a diagnosis of melanoma or dysplastic nevus with severe atypia.[8,14-16] Examples of these dermoscopic features can be found in Fig 1.

The respective positive predictive values of loss of network, branched streaks, and thickened brown lines for melanoma were 18%, 14%, and 11%. The respective positive predictive values of loss of network, branched streaks, and thickened brown lines for melanoma or severely dysplastic nevus were 46%, 29%, and 28%. These values were significantly lower than observed for shiny white streaks or inverse pigment network. In patients with dysplastic nevus syndrome and many atypical nevi, this translates to only 1 potential melanoma diagnosis out of every 10 biopsied lesions with thickened brown lines. Hence in dysplastic nevus patients, these network aberrations found in isolation may not be sufficient to indicate a biopsy, and other dermoscopic and clinical factors will likely be needed to help determine the decision to biopsy. Examples of these dermoscopic features are shown in Fig 2.

A number of statistically significant histologic correlates to the dermoscopic features studied were identified. Thickened brown lines were statistically correlated with increased pigmentation in the epidermis. This is expected because melanin pigment in the lower epidermis typically is brown.[8] Because increased pigment in the epidermis can be the result of melanocyte activation with increased pigment production without necessarily having a significant increase in the number of melanocytes, it is not unanticipated that this particular network abnormality had a lower specificity than some of the others studied. An inverse pigment network had a statistically significant correlation with the

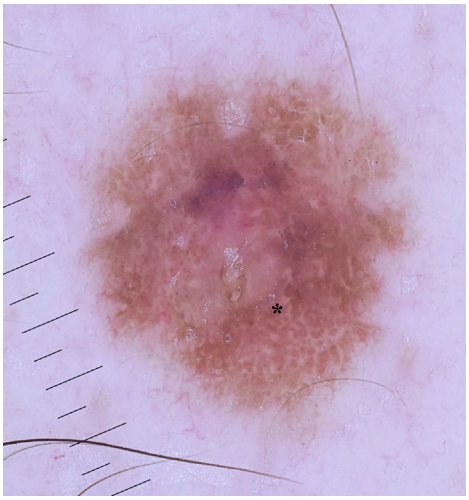

Fig 1. Melanoma in situ. Pigmented lesion from the chest of a 30-year-old man. There are minute foci of residual reticular network at the periphery of the lesion. Shiny white lines can be observed throughout, most obviously at the 6 o'clock region, which are converging to form an inverse pigment pattern, indicated by the asterisk. Pathology showed melanoma in situ arising in a nevus. This combination of shiny white lines and inverse pigment network was the most predictive of melanoma.

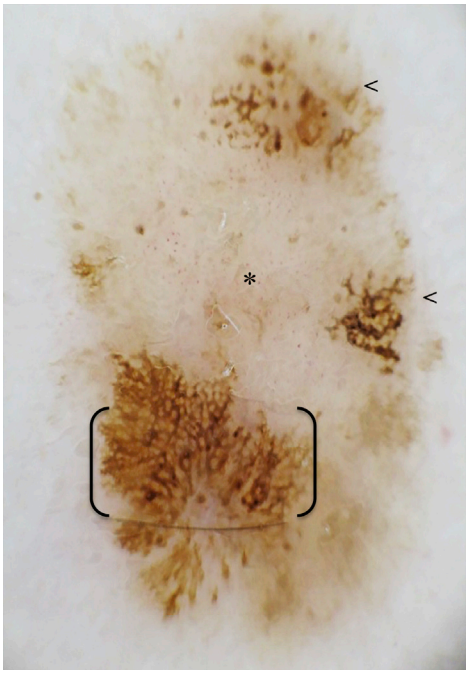

Fig 2. Melanoma in situ. This pigmented lesion shows a combination of loss of network toward the center (asterisk), branched streaks at 12 and 3 o'clock (ar), and some thickened brown lines at 6 o'clock (brackets). The presence of multiple features increases the likelihood of melanoma. This case showed changes of melanoma in situ on pathology. However, the presence of any of these 3 features individually had a considerably lower positive predictive value for melanoma than shiny white streaks or inverse pigment network.

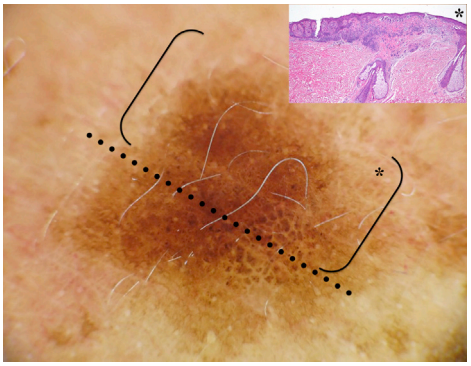

Fig 3. Melanoma arising in a nevus. Dermoscopy of a pigmented lesion from the shoulder of an adult woman. There is a reticulated pigment network in the majority of the lesion, but in the 3 to 6 o'clock region, there is an inverse pigment network. The lesion was sectioned to a capture a plane of sectioning that crossed through both the area of reticulation and inverse pigment network, as shown by the dotted line and brackets. The asterisk on the dermoscopic and histologic images denotes directional alignment. The pathology showed a melanoma arising in a background nevus, with the melanoma being based in the area of inverse pigment. The nevus component in the area of reticulation on the left-hand side of the pathology inset shows a normal rete pattern. The area of inverse pigment has loss of the normal rete pattern with large expansile nests and only small thin spaces between the large nests.

presence of increased fibroplasia and expansile nests. The regular pigment network is formed by aggregation of pigment around the rete ridges.[17] We speculate that the presence of expansile nests with pigment results in an increase in the relative pigmented region assessed by dermoscopy, leaving only irregular curvilinear lines of the nonpigmented region that is the space between the expansile nests of pigmented melanocytes. This dermoscopic histologic correlate is illustrated in Fig 3. Shiny white streaks were associated with fibroplasia. This has been previously described, and it is presumed that the thickened collagen from stromal response to the tumor refracts light, resulting in the shiny white structures.[8,14-16]

This study describes the histologic correlates and utility of specific network aberrations in diagnosing melanoma and severely dysplastic nevi, particularly in patients with many dysplastic nevi. A limitation of the study is that a single reviewer assessed the dermoscopic and histologic features. The sample size is also a limitation and acral or facial lesions were not included in the study. Inverse network pattern or the presence of shiny white streaks had very high predictive value for a diagnosis of melanoma or severely dysplastic nevus, and the presence of 1 of these abnormalities should prompt a biopsy. The

presence of loss of network, thickened brown lines, or branched streaks as isolated findings without other dermoscopic abnormalities needs to be considered in the context of the patient and other risk factors.

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