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Dermoscopic diagnosis of amelanotic/hypomelanotic melanoma

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DEAR EDITOR,

Amelanotic/hypomelanotic melanoma (AHM) is a subtype including melanomas with little or no melanin pigmentation, amelanotic melanoma (AM); it represents 2-8 % of all melanomas.\textsuperscript{1,2} AM may be difficult to diagnose because of lack of pigmentation and symmetry: recently, germline mutations have been reported in the MC1R gene and to a certain extent also in the MITF gene.\textsuperscript{3}

Few studies have described the dermoscopic features of thin (≤ 1 mm) and thick (> 1 mm) AHM; this latter compared with thin AHM showed a greater frequency of hairpin, peripheral vessels, large blue-gray ovoid nests, central vessels, ulceration, large vessels and pink color.\textsuperscript{2}

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In our previous study, thick vs thin AHM showed a greater frequency of irregular pigmentation and milky-red areas.\(^4\)

In this retrospective study, 184 consecutive histopathologically diagnosed amelanotic/hypomelanotic nodular melanomas (AHNM, 41), amelanotic/hypomelanotic superficial spreading melanomas (AHSSM, 37), and amelanotic/hypomelanotic non-melanocytic lesions (AHNML) plus amelanotic/hypomelanotic benign melanocytic lesions (AHBML), 106 (i.e., 51 basal cell carcinoma, 28 seborrheic keratosis and 27 compound/dermal nevi) from 15 participating Italian centers, during 2007-2011, were dermoscopically evaluated to assess validity of dermoscopy in AHNM detection. The dermoscopic evaluation and statistical analysis have already been described.\(^4\) To quantify the dermoscopic features of AHNM vs. AHSSM and AHNM vs. AHNML and AHBML, unconditional logistic regression models were applied to compute odds ratios (ORs) and corresponding 95% confidence intervals (CIs). The multivariate analysis of dermoscopic features of AHNM vs. AHSSM showed that blue-whitish veil (OR, 5.16) and structureless pattern (OR, 4.45) were significantly, independently associated with AHNM (Table 1). The blue-white veil has already been significantly associated with nodular melanoma (NM) because of its histopathological correlation with melanin in the mid-dermis.\(^6\)

The structureless pattern (devoid or with too few structures to constitute a pattern, except for the presence of blood vessels)\(^7\) may be correlated with reduced structures reported in thick vs thin AHM.\(^2,4\)

When evaluating at multivariate analyses the dermoscopic features of AHNM vs. AHNML and AHBML, we found that structureless pattern (OR, 481.44), hypopigmented pseudo-lacunas (OR, 132.22), polymorphic vessels associated with milky red globules/areas (OR,
little blue-black color (OR, 132.24), polymorphous vessels combined with red 
homogeneous areas (OR, 95.99), and homogeneous disorganized pattern (OR, 117.07) 
were significantly associated with an increased risk of AHNM (Table 1).

Pseudo-lacunas or “clods” may also be found in haemangioma, seborrheic keratosis, dermal 
nevus, melanoma and AHNM; in this latter hypopigmented pseudo-lacunas appeared 
irregular in size, shape, color and distribution. (Figure 1).

We found a greater frequency of polymorphous vessels combined with milky red 
globules/areas and/or red homogeneous areas (structureless areas of red homogeneous 
colour) in AHNMs; these combinations of vascular structures have already been associated 
with > 2 mm thick AHM; in our study, 75.6% of AHNM had a thickness >2 mm and only 
19.5% a thickness (1 -2 mm), in which more frequently dotted and linear irregular vessels 
should be found. Therefore, we did not find a significant presence of dotted and linear 
irregular vessels in this study, differently from our previous.4

Little blue-black color, a combination of two colors involving <10% of lesion surface, may be 
seen on the pink-reddish background along with polymorphous vessels, addressing AHNM 
diagnosis; blue-black color, extending more than 10% was significantly associated with 
pigmented NM.5

The homogeneous disorganized pattern, found in AHNM, may be differentiated from 
homogeneous pink pigmentation seen in common nevi in very fair skinned persons, because 
of more shades of pink, asymmetrically distributed intermixed with polymorphous vessels 
and milky red areas/globules (Fig. 1).
Dermoscopy may be useful for the diagnosis of AHNM, thanks to visualization of features associated with deep tumor extension (blue-whitish veil, polymorphous vessels, little blue-black color, pseudo-lacunas) not visible to the naked eye.

However, thin AM or pink melanoma were dermoscopically more difficult to diagnose than pink thick melanomas because we found high sensitivity (87.8%) and high specificity (87.7%) to correctly classify AHNM as melanoma, but a lower sensitivity (51.4%) to correctly classify AHSSM as melanoma. This may depend on higher percentage of AM, 28 out 37 (75.7%) among AHSSM, differently from our previous study in which only 10 out of 44 (23%) were AM, while (77%) were hypomelanotic, easier to diagnose (sensitivity and specificity for all AHMs irrespective of nodular or SSM were 89% and 96% respectively).4

The accuracy of AM dermoscopic diagnosis could increase with the help of reflectance confocal microscopy (RCM);11 a combined approach should result in accurate AM diagnoses.3

Our study limitations regarding the retrospective design, the limited selection of control group diagnoses, and different dermoscopy used (i.e., 63.1% and 36.9% of images were taken with a camera using non-polarized and polarized dermoscopy respectively, and the rest had missing information, influencing the visualization of vessels, red areas, and shiny white lines, better visualized with polarized dermoscopy),12 do not allow drawing firm conclusions on the leading role of dermoscopy in AHM detection.
Acknowledgments

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References


Figure Legend

Fig 1. Amelanotic/hypomelanotic nodular melanoma. (a) In the clinical image of this 2.5 mm thick AHM located on the right leg of a 21-year-old man, a shiny pink reddish symmetrical nodule can be observed (inserts). Dermoscopically, the melanoma reveals a diffuse homogeneous disorganized pigmentation with different shades of pink asymmetrically distributed, intermixed with polymorphous vascular pattern including dotted (small arrow), linear irregular, (large arrow), irregular hairpin (small top arrows), milky red areas (asterisk) and hypopigmented pseudo-lacunas (arrowheads) irregular in size, shape and distribution.
In addition, irregular brown globules/dots and white shiny lines can also be observed, as clue features to add to the above cited criteria in differentiating AHNM from other lesions.
Table 1. Most frequent dermoscopic features of AHNM versus AHSSM and of AHNM versus AHBML+AHNNM: Univariate and multivariate analyses of 184 amelanotic/hypomelanotic skin lesions

<table>
<thead>
<tr>
<th>Dermoscopic features</th>
<th>AHNM (N. 41)</th>
<th>AHSSM (N. 37)</th>
<th>Univariate OR (95% CI)¹</th>
<th>Multivariate² OR (95% CI)²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue-whitish veil</td>
<td>14 (34.2)</td>
<td>5 (13.5)</td>
<td>3.32 (1.06-10.40)</td>
<td>5.16 (1.32-20.25)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p=0.04</td>
<td>p=0.02</td>
</tr>
<tr>
<td>Structureless pattern</td>
<td>27 (65.9)</td>
<td>16 (43.2)</td>
<td>2.53 (1.01-6.33)</td>
<td>4.45 (1.46-13.58)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p=0.05</td>
<td>p=0.009</td>
</tr>
<tr>
<td>Polymorphous vessels + milky red globules/areas</td>
<td>9 (22.9)</td>
<td>2 (5.4)</td>
<td>4.92 (0.99-24.51)</td>
<td>3.93 (0.68-22.63)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p=0.05</td>
<td>p=ns</td>
</tr>
</tbody>
</table>

AHNM AHBML + AHNML
(N. 41) (N. 106)

N. (%) N. (%)

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<table>
<thead>
<tr>
<th>Pattern</th>
<th>Cases</th>
<th>Controls</th>
<th>Median (IQR)</th>
<th>Mean (IQR)</th>
<th>p-value 1</th>
<th>p-value 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structureless pattern</td>
<td>27 (65.9)</td>
<td>10 (9.4)</td>
<td>18.51 (7.40-46.30)</td>
<td>481.44 (14.26-995.55)</td>
<td>&lt;0.0001</td>
<td>0.0006</td>
</tr>
<tr>
<td>Hypopigmented pseudo lacunas</td>
<td>19 (46.3)</td>
<td>6 (5.7)</td>
<td>14.39 (5.15-40.20)</td>
<td>138.22 (6.73-995.55)</td>
<td>&lt;0.0001</td>
<td>0.001</td>
</tr>
<tr>
<td>More one shade of pink</td>
<td>16 (39.0)</td>
<td>5 (4.7)</td>
<td>12.93 (4.32-38.65)</td>
<td></td>
<td>&lt;0.0001</td>
<td>ns</td>
</tr>
<tr>
<td>Blue-whitish veil</td>
<td>14 (34.2)</td>
<td>7 (6.6)</td>
<td>7.33 (2.69-19.98)</td>
<td></td>
<td>&lt;0.0001</td>
<td>ns</td>
</tr>
<tr>
<td>Shiny white lines</td>
<td>20 (48.8)</td>
<td>15 (14.2)</td>
<td>5.78 (2.54-13.13)</td>
<td></td>
<td>&lt;0.0001</td>
<td>ns</td>
</tr>
<tr>
<td>Asymmetric pigmentation</td>
<td>32 (78.1)</td>
<td>44 (41.5)</td>
<td>5.00 (2.18-11.54)</td>
<td></td>
<td>0.0002</td>
<td>ns</td>
</tr>
<tr>
<td>Irregular blotches</td>
<td>11 (26.8)</td>
<td>4 (3.8)</td>
<td>9.35 (2.78-31.49)</td>
<td></td>
<td>0.0003</td>
<td>ns</td>
</tr>
<tr>
<td>Irregular dots/globules</td>
<td>21 (51.2)</td>
<td>21 (19.8)</td>
<td>4.25 (1.96-9.24)</td>
<td></td>
<td>0.0003</td>
<td>ns</td>
</tr>
<tr>
<td>Regression structures</td>
<td>16 (39.0)</td>
<td>13 (12.3)</td>
<td>4.58 (1.95-10.76)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feature</td>
<td>Count</td>
<td>%</td>
<td>Odds Ratio (CI)</td>
<td>p Value</td>
<td>p Value</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------</td>
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</tr>
<tr>
<td>Black color</td>
<td>9 (22.0)</td>
<td>2 (1.9)</td>
<td>14.62 (3.00-71.18)</td>
<td>p=0.0005</td>
<td>p=ns</td>
<td></td>
</tr>
<tr>
<td>Polymorphous vessels + milky red globules/areas</td>
<td>9 (22.0)</td>
<td>1 (0.9)</td>
<td>29.53 (3.60-242.01)</td>
<td>p=0.002</td>
<td>p=0.007</td>
<td></td>
</tr>
<tr>
<td>Little blue-black color</td>
<td>7 (17.1)</td>
<td>1 (0.9)</td>
<td>21.62 (2.09-154.72)</td>
<td>p=0.009</td>
<td>p=0.05</td>
<td></td>
</tr>
<tr>
<td>Polymorphous vessels + red homogeneous areas</td>
<td>6 (14.6)</td>
<td>1 (0.9)</td>
<td>18.00 (2.09-154.72)</td>
<td>p=0.009</td>
<td>p=0.03</td>
<td></td>
</tr>
<tr>
<td>Homogeneous disorganized pattern</td>
<td>6 (14.6)</td>
<td>3 (2.8)</td>
<td>5.89 (1.40-24.79)</td>
<td>p=0.02</td>
<td>p=0.005</td>
<td></td>
</tr>
</tbody>
</table>

AHNM=amelanotic/hypomelanotic nodular melanoma; AHSSM=amelanotic/hypomelanotic superficial spreading melanoma; AHBML=amelanotic/hypomelanotic benign melanocytic lesions; AHNML=amelanotic/hypomelanotic nonmelanocytic lesions. ¹Odds ratio (OR) and 95% confidence interval (CI). ²Unconditional logistic regression including all significant features in the univariate analysis. ns=no significant. p value ≤0.05 was considered statistically significant.

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