Dermoscopic diagnosis of amelanotic/hypomelanotic melanoma

Dear Editor, Amelanotic/hypomelanotic melanoma (AHM) is a subtype of melanoma including ones with little or no melanin pigmentation – amelanotic melanoma (AM). It represents 2–8% of all melanomas.[1,2] AM may be difficult to diagnose because of lack of pigmentation and presence of symmetry. Recently, associated germline mutations have been reported in the *MC1R* gene, and to a certain extent also in the *MITF* gene.[3,4]

Few studies have described the dermoscopic features of thin (≤ 1 mm) and thick (> 1 mm) AHM; compared with thin AHM these show a greater frequency of hairpin, peripheral vessels, large blue-grey ovoid nests, central vessels, ulceration, large vessels and pink colour.[2] In our previous study, thick vs. thin AHM showed a greater frequency of irregular pigmentation and milky-red areas.[5]

This retrospective study included 184 consecutive histopathologically diagnosed amelanotic/hypomelanotic nodular melanomas (AHNMs, n = 41), amelanotic/hypomelanotic superficial spreading melanomas (AHSSMs, n = 37) and amelanotic/hypomelanotic nonmelanocytic lesions (AHNMLs), plus amelanotic/hypomelanotic benign melanocytic lesions (AHBMLs, n = 106: 51 basal cell carcinoma, 28 seborrhoeic keratosis and 27 compound/dermal naevi). These were identified at 15 participating Italian centres during 2007–2011 and were dermoscopically evaluated to assess the validity of dermoscopy in AHNM detection.

The dermoscopic evaluation and statistical analysis have already been described.[5,6] To quantify the dermoscopic features of AHNM vs. AHSSM and AHNM vs. AHNML + AHBML, unconditional logistic regression models were applied to compute odds ratios (ORs) and corresponding 95% confidence intervals. 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). Blue-whitish veil has already been significantly associated with nodular melanoma (NM) because of its histopathological correlation with melanin in the mid-dermis.[7] The structureless pattern (devoid of or with too few structures to constitute a pattern, except for the presence of blood vessels)[8] may be correlated with reduced structures reported in thick vs. thin AHM.[2,4]

When evaluating with multivariate analyses the dermoscopic features of AHNM vs. AHNML + AHBML, we found that: structureless pattern (OR 481·44); hypopigmented pseudolacunas (OR 138·22); polymorphous vessels associated with milky-red globules or areas (OR 296·53); little blue-black colour (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). Pseudolacunas or 'clods' may also be found in haemangioma, seborrhoeic keratosis, dermal naevus, melanoma and AHNM;[9,10] in the latter, hypopigmented pseudolacunas appeared irregular in size, shape, colour and distribution (Fig. 1).

We found a greater frequency of polymorphous vessels combined with milky-red globules or 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.[11] In our study, 75·6% of AHNMs had a thickness > 2 mm and only

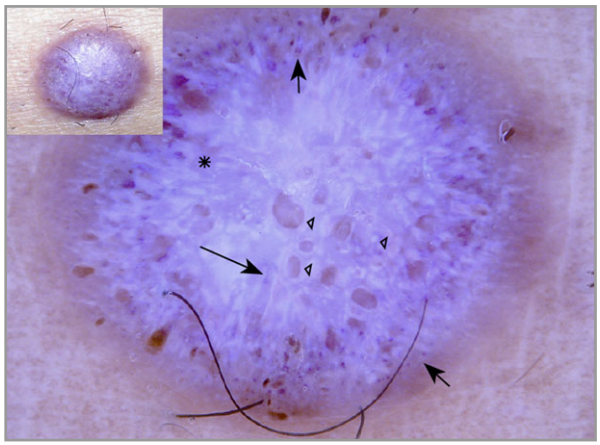

Fig 1. Amelanotic/hypomelanotic nodular melanoma (AHNM). In the clinical image of this 2·5-mm-thick amelanotic/hypomelanotic melanoma located on the right leg of a 21-year-old man, a shiny pink reddish symmetrical nodule can be observed (inset). Dermoscopically, the melanoma reveals a diffuse homogeneous disorganized pigmentation with different shades of pink asymmetrically distributed, intermixed with a polymorphous vascular pattern including dotted (bottom small arrow), linear irregular (large arrow), irregular hairpin (top small arrow) and milky-red areas (asterisk), and hypopigmented pseudolacunas (arrowheads), which are irregular in size, shape and distribution. In addition, irregular brown globules/dots and white shiny lines can also be observed, as additional clues to the above-mentioned criteria in differentiating AHNM from other lesions.

Table 1 The most frequent dermoscopic features of AHNM vs. AHSSM and of AHNM vs. AHBML + AHNML: univariate and multivariate analyses of 184 amelanotic/hypomelanotic skin lesions

			Univariate	Multivariate[b]
Dermoscopic features	AHNM (n = 41)[a]	AHSSM (n = 37)[a]	OR (95% CI) and P-value	
Blue-whitish veil	14 (34)	5 (14)	3·32 (1·06–10·40) 0·04	5·16 (1·32–20·25) 0·02
Structureless pattern	27 (669)	16 (43)	2·53 (1·01–6·33) 0·05	4·45 (1·46–13·58) 0·009
Polymorphous vessels + milky-red globules/areas	9 (23)	2 (5)	4·92 (0·99–24·51) 0·05	3·93 (0·68–22·63) NS
	AHNM (n = 41)	AHBML + AHNML (n = 106)		
Structureless pattern	27 (66)	10 (9·4)	18·51 (7·40–46·30) < 0·001	481·44 (14·26–995·55) < 0·001
Hypopigmented pseudolacunas	19 (46)	6 (5·7)	14·39 (5·15–40·20) < 0·001	138·22 (6·73–995·55) 0·001
More than one shade of pink	16 (39)	5 (4·7)	12·93 (4·32–38·65) < 0·001	NS
Blue-whitish veil	14 (34)	7 (6·6)	7·33 (2·69–19·98) < 0·001	NS
Shiny white lines	20 (49)	15 (14·2)	5·78 (2·54–13·13) < 0·001	NS
Asymmetric pigmentation pattern	32 (78)	44 (41·5)	5·00 (2·18–11·54) < 0·001	NS
Irregular blotches	11 (27)	4 (3·8)	9·35 (2·78–31·49) < 0·001	NS
Irregular dots/globules	21 (51)	21 (19·8)	4·25 (1·96–9·24) < 0·001	NS
Regression structures	16 (39)	13 (12·3)	4·58 (1·95–10·76) < 0·001	NS
Black colour	9 (22)	2 (1·9)	14·62 (3·00–71·18) < 0·001	NS
Polymorphous vessels + milky red globules/areas	9 (22)	1 (0·9)	29·53 (3·60–242·01) 0·002	296·53 (11·05–995·55) < 0·001
Little blue-black colour	7 (17)	1 (0·9)	21·62 (2·09–154·72) 0·009	132·24 (0·92–995·55) 0·05
Polymorphous vessels + red homogeneous areas	6 (15)	1 (0·9)	18·00 (2·09–154·72) 0·009	95·99 (1·49–995·55) 0·03
Homogeneous disorganized pattern	6 (15)	3 (2·8)	5·89 (1·40–24·79) 0·02	117·07 (4·15–995·55) 0·005

AHNM, amelanotic/hypomelanotic nodular melanoma; AHSSM, amelanotic/hypomelanotic superficial spreading melanoma; AHBML, amelanotic/hypomelanotic benign melanocytic lesion; AHNML, amelanotic/hypomelanotic nonmelanocytic lesion; OR, odds ratio; CI, confidence interval; NS, not significant. [a]Values are n (%). [b]Unconditional logistic regression including all significant features in the univariate analysis. P-values ≤ 0·05 were considered statistically significant.

19·5% had a thickness 1–2 mm, in which dotted and linear irregular vessels should be found more frequently. Therefore, we did not find a significant presence of dotted and linear irregular vessels in this study, differently from our previous results.[5]

Little blue-black colour, a combination of two colours involving < 10% of the lesion surface, may be seen on the pink-reddish background along with polymorphous vessels, addressing AHNM diagnosis; blue-black colour extending > 10% was significantly associated with pigmented NM.[6] The homogeneous disorganized pattern found in AHNM may be differentiated from the homogeneous pink pigmentation seen in common naevi in very fair-skinned persons because of more shades of pink, asymmetrically distributed vessels intermixed with polymorphous vessels, and milky-red areas or globules (Fig. 1).

Dermoscopy may be useful in the diagnosis of AHNM, thanks to visualization of features associated with deep tumour extension (blue-whitish veil, polymorphous vessels, little blue-black colour, pseudolacunas) not visible to the naked eye. However, thin AMs or pink melanomas were dermoscopically more difficult to diagnose than pink thick melanomas, and we found high sensitivity (87·8%) and high specificity (87·7%) to classify AHNM correctly as melanoma, but a lower sensitivity (51·4%) to classify AHSSM correctly as melanoma. This may depend on the higher percentage of AMs among AHSSMs (28 of 37, 76%), differently from our previous study in which only 10 of 44 (23%) were AM, while 77% were

hypomelanotic and easier to diagnose (the sensitivity and specificity for all AHMs irrespective of being nodular or SSM were 89% and 96%, respectively).[5]

The accuracy of AM dermoscopic diagnosis could increase with the help of reflectance confocal microscopy;[12] a combined approach should result in accurate AM diagnoses.[3]

Our study has limitations regarding the retrospective design, the limited selection of control group diagnoses, and the different methods of dermoscopy used (63·1% and 36·9% of images were taken with a camera using nonpolarized and polarized dermoscopy, respectively). Some lesions had missing information regarding the type of dermoscopy used. Vessels, red areas and shiny white lines, are better visualized with polarized dermoscopy.[13] This prevents us from drawing firm conclusions on a leading role for dermoscopy in AHM detection.

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M.A. Pizzichetta[1]
H. Kittler[2]
I. Stanganelli[3]
G. Ghigliotti[4]
M.T. Corradin[5]
P. Rubegni[6]
S. Cavicchini[7]
V. De Giorgi[8]
R. Bono[9]
M. Alaibac[10]
S. Astorino[11]
F. Ayala[12]
P. Quaglino[13]
G. Pellacani[14]
G. Argenziano[15]
D. Guardoli[14]
F. Specchio[16]
D. Serraino[17]
R. Talamini[17]
on behalf of the Italian Melanoma Intergroup

[1]*Division of Medical Oncology – Preventive Oncology, Centro di Riferimento Oncologico, National Cancer Institute, Aviano, Italy*
[2]*Department of Dermatology, Medical University of Vienna, Vienna, Austria*
[3]*Skin Cancer Unit, Istituto Tumori Romagna (IRST), Meldola, Department of Dermatology, University of Parma, Italy*
[4]*IRCCS San Martino – 1st Clinic of Dermatology, Genova, Italy*
[5]*Division of Dermatology, Pordenone Hospital, Pordenone, Italy*
[6]*Department of Dermatology, University of Siena, Siena, Italy*
[7]*Department of Dermatology, Fondazione Ospedale Maggiore Policlinico IRCCS, Milan, Italy*
[8]*Department of Dermatology, University of Florence, Florence, Italy*
[9]*Istituto Dermopatico Immacolata, IRCCS, Rome, Italy*
[10]*Department of Dermatology, University of Padova, Italy*
[11]*Division of Dermatology, Celio Hospital, Rome, Italy*
[12]*National Cancer Institute, 'Fondazione G. Pascale'-IRCCS, Naples, Italy*
[13]*Dermatologic Clinic, Department of Medical Sciences, University of Torino, Torino, Italy*
[14]*Department of Dermatology, University of Modena and Reggio Emilia, Modena, Italy*
[15]*Dermatology Unit, Second University of Naples, Naples, Italy*
[16]*Skin Cancer Unit, Arcispedale Santa Maria Nuova IRCCS, Reggio Emilia, Italy*
[17]*Unit of Epidemiology and Biostatistics, Centro di Riferimento Oncologico, National Cancer Institute, Aviano, Italy*
E-mail: *pizzichetta@cro.it*

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