British Journal of Dermatology 2004; **150:** 1117–1124. DOI: 10.1111/j.1365-2133.2004.05928.x

Clinical and Laboratory Investigations

Amelanotic/hypomelanotic melanoma: clinical and dermoscopic features

M.A.PIZZICHETTA, R.TALAMINI,* I.STANGANELLI,† P.PUDDU,‡ R.BONO,‡ G.ARGENZIANO,§ A.VERONESI, G.TREVISAN,¶ H.RABINOVITZ** AND H.P.SOYER††

Division of Medical Oncology C–Preventive Oncology, Centro di Riferimento Oncologico, Aviano, Via Pedemontana Occidentale 12, I-33081 Aviano, Italy
**Epidemiology Unit, Centro di Riferimento Oncologico, Aviano, Italy*
†Skin Cancer Unit, Ravenna–Niguarda Hospital, Milano, Italy
‡Department of Onco-Immunodermatology, IDI, Rome, Italy
§Department of Dermatology, Second University of Naples, Italy
¶Department of Dermatology, University of Trieste, Italy
***Department of Dermatology, University of Miami, USA*
††Department of Dermatology, University of Graz, Austria

Accepted for publication 5 November 2003

Summary

Background Amelanotic malignant melanoma is a subtype of cutaneous melanoma with little or no pigment on visual inspection. It may mimic benign and malignant variants of both melanocytic and nonmelanocytic lesions.

Objectives To evaluate whether dermoscopy is also a useful technique for the diagnosis of amelanotic/hypomelanotic melanoma (AHM).

Methods We conducted a retrospective clinical study of 151 amelanotic/hypomelanotic skin lesions from 151 patients with a mean age of 47 years (± 17·5 SD). Digitized images of amelanotic/hypomelanotic skin lesions were converted to JPEG format and sent by e-mail from the five participating centres. Lesions included 55 amelanotic/hypomelanotic nonmelanocytic lesions (AHNML), 52 amelanotic/hypomelanotic benign melanocytic lesions (AHBML), and 44 AHM, 10 (23%) of which were nonpigmented, truly amelanotic melanomas (AM). The 44 AHM lesions were divided into thin melanomas (TnM) ≤ 1 mm (29 cases) and thick melanomas (TkM) > 1 mm (15 cases), according to the Breslow index. Five clinical features (elevation, ulceration, shape, borders and colour) as well as 10 dermoscopic criteria (pigment network, pigmentation, streaks, dots/globules, blue-whitish veil, regression structures, hypopigmentation, leaf-like areas, multiple grey-bluish globules, central white patch) and eight vascular patterns (comma, arborizing, hairpin, dotted, linear irregular, dotted and linear irregular vessels, and milky-red areas) were evaluated in order to achieve clinical and dermoscopic diagnoses. Statistical analyses were performed with the χ^2-test and Fisher's exact test, when appropriate.

Results The most frequent and significant clinical features for TnM and TkM were asymmetry and ulceration (the latter only for TkM) compared with AHBML. Irregular dots/globules (62% vs. 35%; $P \leq 0{\cdot}03$), regression structures (48% vs. 27%; $P \leq 0{\cdot}03$), irregular pigmentation (41% vs. 11%; $P \leq 0{\cdot}03$) and blue-whitish veil (10% vs. 0%; $P \leq 0{\cdot}03$) were the most relevant dermoscopic criteria for TnM in comparison with AHBML. TkM differed significantly from AHBML in frequency of occurrence of irregular pigmentation (87% vs. 11%; $P \leq 0{\cdot}03$), irregular dots/globules (73% vs. 35%; $P \leq 0{\cdot}03$), regression structures (67% vs. 27%; $P \leq 0{\cdot}03$), blue-whitish veil (27% vs. 0%; $P \leq 0{\cdot}03$) and hypopigmentation (13% vs. 55%; $P \leq 0{\cdot}03$). Linear irregular vessels and the

Correspondence: Maria Antonietta Pizzichetta.
E-mail: pizzichetta@cro.it

combination of dotted and linear irregular vessels associated with TnM and TkM were not found in our cases of AHBML and were only rarely seen in AHNML (3·6% and 1·8%, respectively). Moreover, TkM differed significantly from AHBML and TnM in frequency of occurrence of milky-red areas (93% vs. 17%; $P \leq 0{\cdot}03$ and 93% vs. 31%; $P \leq 0{\cdot}01$, respectively). The dermoscopic diagnosis of melanoma had a higher sensitivity and specificity than the clinical diagnosis (89% and 96% vs. 65% and 88%, respectively). With the limitation of the small number of cases, vascular patterns were the only dermoscopic criteria for 'truly' AM. In the 10 cases of 'truly' AM, we found milky-red areas in more than half of the cases (six of 10), dotted vessels in four, hairpin vessels in two, linear irregular vessels in two, dotted and linear irregular vessels in two.

Conclusions Because dermoscopy uses criteria reflecting pigmentation (irregular pigmentation and irregular dots/globules) and vascular patterns, it is a useful technique not only for pigmented melanoma but also for hypomelanotic melanoma. In 'truly' AM, vascular patterns alone may not be sufficient to diagnose melanoma. A combined approach with the clinical information should help in the detection of 'truly' AM.

Key words: amelanotic melanoma, dermatoscopy, dermoscopy, epiluminescence microscopy, melanocytic skin lesion, nonmelanocytic skin lesions

Amelanotic malignant melanoma is a subtype of cutaneous melanoma with little or no pigment at visual inspection.[1,2] A review of the literature indicates that amelanotic melanomas (AM) represent 2–8% of all malignant melanomas; the precise incidence is difficult to calculate as the term amelanotic is often used to indicate melanomas only partially devoid of pigment.[3] 'Truly' AM are rare; often some pigmentation is present at the periphery of the lesion, and the amelanotic/hypomelanotic melanoma (AHM) mimics benign and malignant variants of both melanocytic and nonmelanocytic lesions.[2] We conducted a study to learn more about the clinical and dermoscopic features of this rare melanoma and to investigate the possibility of using dermoscopy to differentiate it from amelanotic/hypomelanotic benign melanocytic lesions (AHBML) and from amelanotic/hypomelanotic nonmelanocytic lesions (AHNML).

Amelanotic malignant melanoma tends to occur in sun-exposed skin, especially in elderly persons with photodamage, and may appear as erythematous, sometimes scaly, macules or plaques with irregular borders, simulating benign inflammatory plaques, superficial basal cell carcinoma (BCC), actinic keratosis, Paget's or Bowen's disease.[4–8] It may also present with translucent papules, thereby resembling BCC, or it may clinically resemble keratoacanthoma or Merkel cell carcinoma.[4,9] Alternatively, it may present as an exophytic nodule, often eroded, simulating a pyogenic granuloma or haemangioma, or as a skin-coloured dermal plaque/nodule known as desmoplastic malignant melanoma.[4,10,11]

Dermoscopy (dermatoscopy, epiluminescence microscopy, incident light microscopy and surface microscopy) is a noninvasive technique that has been introduced as an additional measure to increase the accuracy of diagnosing pigmented skin lesions and to improve the sensitivity and specificity for diagnosing melanoma.[12,13] In this retrospective study, 151 amelanotic/hypomelanotic skin lesions, including 44 AHM, were examined clinically and dermoscopically to evaluate whether dermoscopy is a useful technique for the diagnosis of AHM.

Materials and methods

All cases of clinical and/or dermoscopic hypomelanotic (extent of pigmentation $\leq 30\%$) and amelanotic skin lesions seen at the five participating centres (four in Italy and one in the U.S.A.) between January 1996 and December 2001 were considered for the study. One hundred and seventy-four images were sent by e-mail to the Department of Medical Oncology–Oncologic Prevention and the Epidemiology Unit of the Centro di Riferimento Oncologico, Aviano, Italy from the five participating centres as follows: the Centre for Cancer Prevention, Ravenna Hospital (27 images); the Department of Immunodermatology, IDI, Rome (34 images); the Department of Dermatology, University of Naples (32 images); the Centro di Riferimento Oncologico, Aviano (52 images); and the Department of Dermatology, University of Miami, FL (29 images). Of these, 122 images were taken with a digital stereomicroscope and 52 were taken with a Dermaphot camera (Heine

Optotechnik; Herrsching, Germany) (× 10 magnification) and then digitalized with the Kodak PhotoCD system. Ultrasound gel was used on all the lesions (52) photographed with the Dermaphot in the Aviano centre. The other centres used the digital stereomicroscope consisting of a stereomicroscope and a Sony 3CCD DXC-930P colour video camera. The digital images were taken at a magnification of ×10–20. No vessel compression occurs with this method because the glass plate of the instrument is not placed directly upon the surface of the lesion but at a distance. Conversely, the glass plate on the undersurface of the Dermaphot photo equipment is lightly pressed directly against the lesion surface (which is covered in mineral oil), thereby compressing the small blood vessels. In order to reduce the pressure on the lesion and the compression of the small blood vessels, we took the precaution of putting on the lesion a large amount of ultrasound gel, a contact liquid needing a lower pressure due to its high viscosity.

Two files were provided for each case, one containing the clinical and dermoscopic images converted to JPEG format, and the other containing all patient-related information such as gender, age at diagnosis, skin lesion site and histopathological diagnosis of each lesion. During November and December 2001, the incoming dermoscopic images ($n = 174$) from all five centres were merged in a database with a new identification link to the patient information on clinical features and diagnosis. Of the 174 images submitted, 151 were found to be suitable for the study based on the following two criteria: (i) confirmation of clinical and/or dermoscopic amelanotic/hypomelanotic lesions with extent of pigmentation $\leq 30\%$,[14] and (ii) an image quality sufficiently good for the evaluation of the dermoscopic criteria, particularly vascular patterns. The 151 images were randomly reorganized in a new file containing both the clinical and dermoscopic images for evaluation at the Centro di Riferimento Oncologico, Aviano. A single blinded observer (M.A.P.) evaluated the images using structured questionnaires, investigating clinical features such as elevation, ulceration, shape, borders, colour and dermoscopic criteria to achieve both a clinical and a dermoscopic diagnosis. The images were coded with unique identification numbers, and only the gender, age at diagnosis and the site of the skin lesion were known to the observer.

Dermoscopic analysis

We used the classic diagnostic approach for dermoscopic diagnosis of pigmented skin lesions known as 'pattern analysis', which is based on the simultaneous and subjective assessment of dermoscopic criteria. Pattern analysis correlates individual criteria with each other and puts them into the context of a pattern that is typical for a specific pathology and, thus, a lesion.[15] We examined all the dermoscopic images to evaluate the frequency of specific dermoscopic criteria in AHNML, AHBML, AHM and 'truly' AM and to analyse the possible relationship between these criteria and the vertical tumour thickness of AHM and 'truly' AM. We assessed the lesions using the following dermoscopic criteria associated with melanoma and nonmelanocytic skin lesions: pigment network, pigmentation, streaks, dots/globules, blue-whitish veil, regression structures, hypopigmentation, leaf-like areas, multiple grey-bluish globules, central white patch and vascular pattern.[16–18]

Statistical analysis

Statistical analyses were performed with the χ^2 test and Fisher's exact test, when appropriate, to evaluate the differences between the various types of lesions in terms of the frequency of occurrences of clinical features, dermoscopic criteria and vascular patterns.[19] Differences were considered to be statistically significant when $P \leq 0{\cdot}05$ (two-sided). To evaluate the efficiency of the tests (dermoscopic diagnosis and clinical diagnosis), for each value we estimated the sensitivity (the ratio between true positives and the sum of true positives and false negatives) and specificity (the ratio between true negatives and the sum of true negatives and false positives). Correlation coefficients were calculated using Spearman's rank correlation methods (Spearman's rank correlation $= r$). Results were considered to be statistically significant when $P \leq 0{\cdot}05$.

Sensitivity was plotted vs. '100 − specificity' to produce a receiver-operating characteristic (ROC) curve. The diagnostic efficiency was estimated as the area under the ROC curve.[20]

Results

Patient demographics and classification of lesions

The patient population consisted of 73 males and 78 females with a mean age of 47 years (± 17·5 SD). The sites of the amelanotic/hypomelanotic skin lesions were: the lower limb (38 patients), back (32 patients), trunk (31 patients), upper limb (18 patients), abdomen (17 patients), head and neck (eight patients), hand (five

patients) and foot (two patients). The series included 55 cases of AHNML, 52 cases of AHBML and 44 cases of AHM. The 55 cases of AHNML consisted of 25 cases of BCC, 10 cases of dermatofibroma, eight cases of Bowen's disease, eight cases of seborrhoeic keratosis and four cases of squamous cell carcinoma (SCC). The 52 cases of AHBML consisted of 24 cases of compound naevi, 17 cases of dermal naevi, five cases of Spitz naevi, four cases of congenital naevi and two cases of combined naevi.

The 44 patients with AHM were 21 males and 23 females with a mean age of 50 years (± 16·7 SD). The distribution of the sites of melanoma was: trunk (18 patients), lower limb (17 patients) and upper limb (nine patients). The series consisted of 10 cases (23%) of nonpigmented, 'truly' AM, of which two cases were desmoplastic melanomas, and 34 cases (77%) were hypopigmented melanomas. Amelanotic and hypomelanotic melanomas histologically presented a partial or total lack of melanin pigment. Cases with regression were excluded. The 44 AHM lesions were subdivided into two groups based on Breslow thickness: ≤ 1 mm, thin melanoma (TnM), 29 cases; and > 1 mm, thick melanoma (TkM), 15 cases.

Dermoscopic classification

Table 1 presents the frequency of occurrence of dermoscopic criteria in 151 amelanotic/hypomelanotic skin lesions, according to histopathological diagnosis and tumour thickness (i.e. AHNML, AHBML, TnM and TkM). TnM differed significantly from AHBML in the frequency of occurrence of irregular dots/globules (62% vs. 35%; $P \leq 0{\cdot}03$), regression structures (48% vs. 27%; $P \leq 0{\cdot}03$), irregular pigmentation (41% vs. 11%; $P \leq 0{\cdot}03$), and blue-whitish veil (10% vs. 0%; $P \leq 0{\cdot}03$). TkM differed significantly from AHBML in the frequency of occurrence of irregular pigmentation (87% vs. 11%; $P \leq 0{\cdot}03$), irregular dots/globules (73% vs. 35%; $P \leq 0{\cdot}03$), regression structures (67% vs. 27%; $P \leq 0{\cdot}03$), blue-whitish veil (27% vs. 0%; $P \leq 0{\cdot}03$) and hypopigmentation (13% vs. 55%; $P \leq 0{\cdot}03$). Similarly, when we used correlation coefficients (Spearman's rank correlation), we found a

Table 1. Frequency of occurrence of some dermoscopic criteria and some vascular patterns in 151 amelanotic/hypomelanotic skin lesions by histopathological diagnosis

	Melanocytic lesions								
	AHNML ($n = 55$)		AHBML ($n = 52$)		TnM (≤ 1 mm) ($n = 29$)[a]		TkM (> 1 mm) ($n = 15$)		Spearman coefficient (r)
	n	%	n	%	n	%	n	%	
Dermoscopic criteria									
Atypical pigment network	0	(0·0)	6	(11·5)	5	(17·2)[b]	0	(0·0)	(0·16)
Irregular pigmentation	2	(3·6)	6	(11·5)	12	(41·4)[b,c]	13	(86·7)[b–d]	(0·53)[h]
Irregular dots/globules	7	(12·7)	18	(34·6)	18	(62·1)[b,c]	11	(73·3)[b,c]	(0·45)[h]
Blue-whitish veil present	1	(1·9)	0	(0·0)	3	(10·3)[c]	3	(26·7)[b,c]	(0·22)[h]
Regression structures	2	(3·6)	14	(26·9)	14	(48·3)[b,c]	10	(66·6)[b,c]	(0·51)[h]
Hypopigmentation present	6	(11·3)	28	(54·9)	9	(31·0)[b]	2	(13·3)[c]	(0·14)
Leaf-like areas present	5	(9·4)	0	(0·0)	0	(0·0)	0	(0·0)	(−0·22)[h]
Multiple grey-bluish globules present	11	(20·8)	0	(0·0)	1	(3·5)[b]	0	(0·0)	(−0·29)[h]
Central white patch present	10	(19·2)	0	(0·0)	0	(0·0)[b]	0	(0·0)	(−0·32)[h]
Vascular patterns									
Absent	8	(14·6)	13	(25·0)	3	(10·3)	1	(6·7)	(0·01)
Comma vessels	0	(0·0)	12	(23·1)	0	(0·0)[e]	0	(0·0)[e]	(0·04)
Arborizing vessels	9	(16·4)	1	(1·9)	1	(3·5)	0	(0·0)	(−0·23)[h]
Hairpin vessels	6	(10·9)	1	(1·9)	2	(6·9)	1	(6·7)	(−0·08)
Dotted vessels	12	(21·8)	17	(32·7)	8	(27·6)	3	(20·0)	(0·03)
Linear irregular vessels	2	(3·6)	0	(0·0)	3	(10·3)[e]	0	(0·0)	(0·03)
Dotted and linear irregular vessels	1	(1·8)	0	(0·0)	4	(13·8)[b,e]	4	(26·7)[b,e]	(0·28)[h]
Milky-red areas	5	(9·1)	9	(17·3)	9	(31·0)[f]	15	(93·3)[c,f,g]	(0·44)[h]

AHBML, amelanotic/hypomelanotic benign melanocytic lesions; AHNML, amelanotic/hypomelanotic nonmelanocytic lesions; TkM, thick melanomas; TnM, thin melanomas. [a]Five melanoma *in situ* were included; [b]compared with nonmelanocytic lesions, $P \leq 0{\cdot}05$; [c]compared with benign melanocytic lesions, $P \leq 0{\cdot}03$; [d]compared with melanoma ≤ 1 mm, $P \leq 0{\cdot}02$; [e]compared with benign melanocytic lesions, $P \leq 0{\cdot}05$; [f]compared with nonmelanocytic lesions, $P \leq 0{\cdot}01$; [g]compared with melanoma ≤ 1 mm, $P \leq 0{\cdot}01$; [h]Spearman correlation coefficient (r): $P \leq 0{\cdot}01$.

statistically significant ($P \leq 0{\cdot}01$) positive correlation between histopathological diagnosis and some dermoscopic criteria: irregular pigmentation ($r = 0{\cdot}53$), irregular dots/globules ($r = 0{\cdot}45$), blue-whitish veil ($r = 0{\cdot}22$) and regression structures ($r = 0{\cdot}51$). Conversely, negative correlations emerged among leaf-like areas ($r = -0{\cdot}22$), multiple grey-bluish globules ($r = -0{\cdot}29$) and central white patch ($r = -0{\cdot}32$) (Table 1). An overall correlation within all the dermoscopic criteria was calculated. A significantly positive correlation was found between irregular pigmentation, irregular dots/globules, blue-whitish veil, regression structures and histopathological diagnosis (data not shown). Conversely, negative correlations emerged for leaf-like areas, multiple grey-bluish globules and central white patch (data not shown). In evaluating vascular patterns (Table 1), we observed that linear irregular vessels and the combination of dotted and linear irregular vessels (Fig. 1) associated with TnM and TkM were not found in our cases of AHBML and were only rarely seen in AHNML (3·6% and 1·8%, respectively). Moreover, TkM differed significantly from AHBML and TnM in frequency of occurrence of milky-red areas (Fig. 1) (93% vs. 17%; $P \leq 0{\cdot}03$ and 93% vs. 31%; $P \leq 0{\cdot}01$, respectively). A statistically significant positive correlation was also found between histopathological diagnosis and some vascular patterns: dotted and linear irregular vessels ($r = 0{\cdot}28$) and milky-red areas ($r = 0{\cdot}44$). By contrast, negative correlations were found between arborizing vessels ($r = -0{\cdot}23$) and histopathological diagnosis (Table 1). Overall correlations within all vascular patterns were calculated (data not shown); significantly positive correlations emerged between dotted vessels, linear irregular vessels, milky-red areas and histopathological diagnosis.

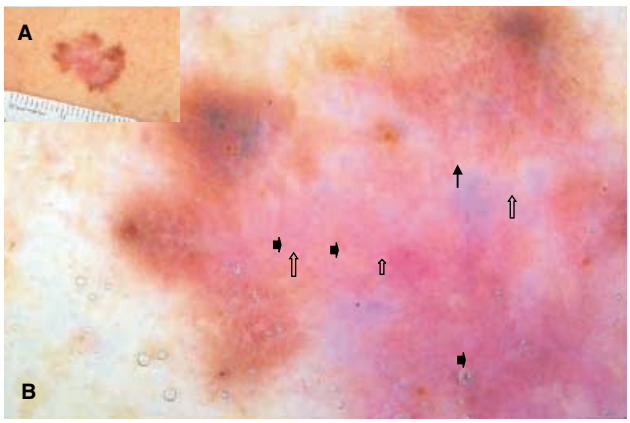

Figure 1. (A) Clinical image of an invasive hypopigmented melanoma, 1·2 mm thick. (B) A dermoscopic image of the same melanoma. Vascular patterns with milky-red areas (↑), combination of dotted (➧) and linear irregular vessels (⇧) associated with other criteria such as irregular pigmentation, irregular dots and regression structures, seen at the periphery of the lesion, suggest a diagnosis of melanoma.

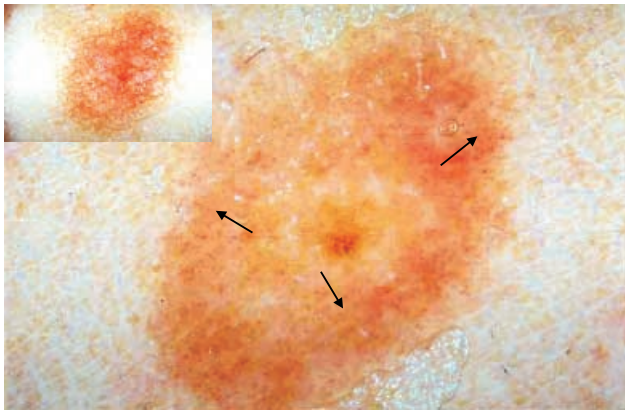

Figure 2. (A) Clinical image of truly amelanotic desmoplastic melanoma, 0·63 mm thick. (B) With dermoscopy, the only criterion identified in this lesion is the presence of dotted vessels (solid arrow), ↑ which alone may not to be sufficient to diagnose melanoma because dotted vessels can be found in common naevi and nonmelanocytic lesions.

The vascular patterns were the only dermoscopic criteria for 'truly' AM. In the 10 cases of 'truly' AM we found milky-red areas in six cases, dotted vessels in four (Fig. 2), hairpin vessels in two, linear irregular vessels in two, dotted plus linear irregular vessels in two. Eight of these 10 cases were TnM.

Clinical classification

Clinical features of the 151 amelanotic/hypomelanotic skin lesions could be evaluated only for the 108 lesions for which clinical images were available. These included all TkM and TnM lesions. Most of the 43 lesions without clinical images were benign melanocytic lesions. Table 2 summarizes the clinical features of the 108 skin lesions according to histopathological diagnosis and the classification of the AHM lesions according to tumour thickness. There was a significantly greater frequency of ulceration in TkM lesions (57%) compared with TnM lesions (12%; $P \leq 0{\cdot}05$) or AHBML (3%; $P \leq 0{\cdot}02$). Moreover, a significantly greater incidence of asymmetry was present in the TnM and TkM lesions compared with AHBML (76% and 79% vs. 28%, respectively; $P \leq 0{\cdot}02$). There was also a significantly greater incidence of peripheral

Table 2. Frequency of occurrence of clinical features in the 108 evaluable amelanotic/hypomelanotic skin lesions by histopathological diagnosis

					Melanoma (tumour thickness in mm)			
	AHNML ($n = 40$)		AHBML ($n = 29$)		TnM (≤ 1 mm) ($n = 25$)[a]		TkM (> 1 mm) ($n = 14$)	
Clinical features	*n*	(%)	*n*	(%)	*n*	(%)	*n*	(%)
Elevation								
Flat	26	(65·0)	19	(65·5)	17	(68·0)	4	(28·6)
Dome-shaped	10	(25·0)	8	(27·6)	5	(20·0)	5	(35·7)
Flat and dome-shaped	4	(10·0)	2	(6·9)	3	(12·0)[c]	5	(35·7)[b–d]
Ulceration								
Absent	27	(69·2)	28	(96·6)	22	(88·0)	6	(42·9)
Present	12	(30·8)	1	(3·4)	3	(12·0)	8	(57·1)[c,d]
Shape								
Symmetry	19	(47·5)	21	(72·4)	6	(24·0)	3	(21·4)
Asymmetry	21	(52·5)	8	(27·6)	19	(76·0)[c]	11	(78·6)[c]
Borders								
Sharp	13	(32·5)	7	(25·9)	14	(56·0)	11	(78·6)
Partly sharp	3	(7·5)	4	(14·8)	5	(20·0)	3	(21·4)
Ill-defined	24	(60·0)	16	(59·3)	6	(24·0)[b,c]	0	(0·0)[b,c]
Colour								
Erythematous	19	(47·5)	4	(14·3)	7	(29·2)	2	(14·3)
Flesh-coloured	7	(17·5)	3	(10·7)	0	(0·0)	0	(0·0)
Irregular pigmented	11	(27·5)	13	(46·4)	7	(29·2)	7	(50·0)
Peripheral pigmentation	3	(7·5)	8	(28·6)	10	(41·6)[b]	5	(35·7)[b]

AHBML, amelanotic/hypomelanotic benign melanocytic lesions; AHNML, amelanotic/hypomelanotic nonmelanocytic lesions; TkM, thick melanomas; TnM, thin melanomas. [a]Five melanoma *in situ* were included; [b]compared with nonmelanocytic lesions, $P \leq 0{\cdot}03$; [c]compared with benign melanocytic lesions, $P \leq 0{\cdot}02$; [d]compared with melanoma ≤ 1 mm, $P \leq 0{\cdot}05$.

pigmentation in TnM lesions (42%) and TkM lesions (36%) than in AHNML (7·5%; $P \leq 0{\cdot}03$). Clinically the 10 cases of 'truly' AM appeared as erythematous macules or plaques with sharp borders in half of the cases (five of 10). Asymmetry was present in most cases (seven of 10) and ulceration was present in only two.

Clinical and dermoscopic diagnoses

A clinical diagnosis was made for each of the 108 lesions with clinical images and compared with the histopathological diagnosis. The area under the curve for dermoscopic diagnosis was greater than the one for clinical diagnosis (Fig. 3), and dermoscopic diagnosis of melanoma had a higher sensitivity and specificity than the clinical diagnosis. The sensitivity and specificity of clinical diagnosis of melanoma were 65% and 88%, respectively. Thirty-five per cent of melanoma cases (13 cases) were clinically misdiagnosed as benign melanocytic lesions (eight cases), BCC (four cases) and Bowen's disease (one case). By contrast, the sensitivity and specificity of dermoscopic diagnosis of melanoma were 89% and 96%, respectively. In clinically evaluating the 10 cases of 'truly' AM we found that eight of these were misdiagnosed as benign melanocytic lesions (five cases) or BCC (three cases). Only four of these 10 cases were correctly diagnosed by the dermoscopic diagnosis; the other six

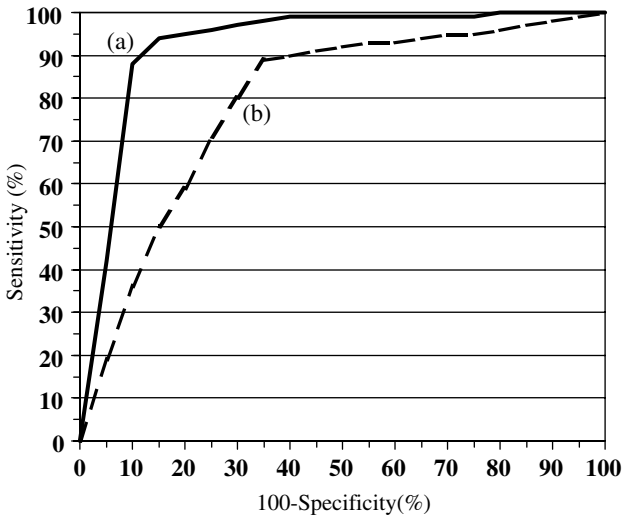

Figure 3. Receiver-operating characteristic (ROC) curves evaluating sensitivity and specificity of (a) dermoscopic diagnosis and (b) clinical diagnosis of melanoma.

were diagnosed as either benign melanocytic lesion (four cases) or BCC (two cases).

Discussion

Our results show that clinical features routinely used for diagnosing melanoma, such as peripheral pigmentation, ulceration and asymmetry, are not really helpful in diagnosing AHM. Peripheral pigmentation is a feature not only of hypopigmented melanoma but also of hypopigmented benign melanocytic lesions, and ulceration and asymmetry were detected both in AHM lesions and in AHNML. Clinical features allowed the correct clinical diagnosis of melanoma in 65% of AHM. More than half the cases of undiagnosed AHM in our study were able to masquerade clinically as AHBML. In 'truly' AM, clinical features do not allow the correct clinical diagnosis of melanoma, which was made in only two of 10 cases, while half (five of 10) of the cases were misdiagnosed as AHBML.

Other authors[21] found a diagnostic sensitivity of 70% for the clinical diagnosis of melanoma, with the remaining 30% of melanomas clinically assessed as false-negative. Common clinical misdiagnoses of AM were naevus, BCC, seborrhoeic keratosis, verruca vulgaris, dermatitis, actinic keratosis, Bowen's disease, keratoacanthoma, dermatofibroma, pyogenic granuloma and haemangioma.[1,8]

When evaluating these amelanotic/hypomelanotic skin lesions dermoscopically, we noted that dermoscopic features which reflect pigmentation such as irregular pigmentation, irregular dots/globules, regression structures and a blue-whitish veil as well as vascular patterns such as milky-red areas, linear irregular vessels or the combination of dotted and linear irregular vessels (Fig. 1) were more prevalent in AHM and were useful in distinguishing AHM from other lesions.

In this series, with the limitation of the small number of cases, dermoscopic criteria for 'truly' AM were vascular patterns. In particular, those more frequently observed in these cases were milky-red areas (six of 10) and dotted vessels (four of 10). However, vascular patterns permitted a correct dermoscopic diagnosis of melanoma in only four of 10 cases, but the small number of 'truly' AM precludes a firm conclusion. Other authors similarly found that vascular patterns can suggest a diagnosis of melanoma when associated with other criteria found in melanocytic lesions (pigment network, streaks, dots/globules).[18] In 'truly' AM, vascular patterns alone (Fig. 2) may not be sufficient to diagnose melanoma because dotted, arborizing, hairpin vessels and even milky-red areas have also been found in common naevi, BCC, seborrhoeic keratosis as well as in melanomas.[18,22]

The patient's medical history and examination of the entire skin surface are very important and must play an important role in the diagnosis and management of 'truly' AM as well as for the so-called 'featureless' melanomas that lack specific surface microscopic features.[23,24] In fact, in our study, all these 'truly' AM had changed in size and had arisen in patients with multiple pigmented lesions and a history of excessive sun exposure. This clinical information led us to excise these 'truly' AM. Routine screening of skin lesions should integrate the dermoscopic evaluation with clinical information such as age, sex, personal or family history of melanoma, number and sites of lesions, time of onset and descriptions of any changes of the lesion over time. A combined approach should result in the detection of 'truly' AM.

Although the present study describes one of the largest series of AHM to date, the small number of 'truly' AM, represented by only 10 cases, is still not sufficient to draw firm conclusions on the vascular patterns of these melanomas. In addition, no training and test set was performed, the study was retrospective and the sample size was not known before the initiation of the study; moreover, the number of SCC cases ($n = 4$) was low.

These retrospective data should be validated in a prospective study which would need an extensive international collaboration to collect a large series of 'truly' AM lesions to identify better the vascular patterns of the rare entities described in this paper.

Acknowledgments

We thank Barbara J.Rutledge and Anna Maria Colussi for their editing assistance.

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