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Dermoscopy of fully regressive cutaneous melanoma

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Conflicts of interest
None declared.

Summary

Background Metastatic melanoma of unknown origin is a difficult challenge diagnostically and therapeutically. Diagnosis of the putative primary lesion is difficult. This difficulty increases when the primary lesion has undergone complete regression.

Objective To define the dermocopic features of fully regressed melanoma.

Patients and methods A single-institution, register-based study of an unselected consecutive series of seven cases of metastatic melanoma in the lymph nodes with no known or visible primary lesion was carried out. Skin examination included dermoscopy; when a suspicious area was found, observed dermoscopic features were recorded and a biopsy was performed. Diagnosis of completely regressive cutaneous melanoma was based on clinical–pathological correlation according to widely accepted criteria.

Results Seven dermoscopic features were associated with completely regressive melanoma: scar-like depigmentation (100%); pink coloration of the background (100%); linear-irregular vessels (86%); globular pattern of the vessels (43%); remnants of pigmentation (86%), either macular (43%) or with a peppering aspect (43%); and white lighter transverse bands (43%). The last feature was only observed with polarized light dermoscopy devices.

Conclusion Dermoscopy more accurately distinguishes the vascular, pigmentary and scarring changes of fully regressive melanoma. We believe that dermoscopy should be included in the search for a regressive primary lesion in case of metastatic melanoma of unknown origin.

Diagnosis of metastatic melanoma at the first examination is not uncommon. In the vast majority of cases the primary cutaneous lesion appears to be obvious when examining the skin of the patient. Features of partial regression of a primary cutaneous melanoma are observed in 10–35% of cases.[1] However, cases of metastatic melanomas with complete regression of the primary cutaneous lesion are quite uncommon and only about 40 cases have been reported in the literature.[2]

From a series of seven cases of metastatic melanoma with a completely regressive histopathology-proven primary lesion we report the dermoscopy features of such lesions and suggest the role of dermoscopy in the management of metastatic melanoma of unknown primary site.

Patients and methods

Patients

The study was performed on a consecutive unselected series of seven cases observed in the Department of Dermatology of Lyon 1 University from 1996 to 2006. The clinical features of the seven cases are summarized in Table 1.

Patient selection from our melanoma database was carried out by using the widely accepted criteria defined by Smith and Stehlin in 1965:[3] (i) all seven patients had histopathology-proven metastatic melanoma at time of initial diagnosis (regional lymph node in all cases); (ii) examination of the whole skin surface of the patient did not reveal any obvious atypical pigmented or unpigmented lesions; (iii) exhaustive study of the patient's medical history did not find any previous cutaneous surgery, and skin examination did not reveal any scar from such a treatment; (iv) systematic specialized ophthalmological, otorhinolaryngological and, when applicable, gynaecological examinations looking for a hidden primary were negative; (v) in all cases a cautious clinical skin examination disclosed a suspicious scar-like lesion that could have been the only remaining symptom of a completely regressive melanoma in the cutaneous area within the drainage zone of the metastatic lymph node (this lesion was systematically biopsied); (vi) in all cases a computed tomography scan of the brain, thorax, abdomen and pelvis, and a lymph node ultrasound were performed at the time of diagnosis and were all negative.

In all seven patients clinical examination was accompanied by dermoscopic examination of the lesion we suspected to

Table 1 Patient characteristics and clinical and pathological features

Patient	Age (years)	Sex	Location	Clinical skin findings	Clinical history of cutaneous lesion	Revealing event	Metastatic disease at time of diagnosis	Pathology of regressive primary lesion
1	63	M	Upper back median (Fig. 1a)	15 mm in diameter, unpigmented lesion with some pigmentation in the periphery on one side (Fig. 1a)	Unknown	Bilateral palpable axillary lymph node	Axillary lymph node R and L (pN2aM0)	Fibroplasia of the dermis with vascular hyperplasia, mild lymphocytic infiltration and perivascular histiocytic infiltration (Fig. 4)
2	38	F	Left upper back	6 mm in diameter, bluish lesion	Unknown	Sus-clavicular enlarged lymph node	Left sus-clavicular lymph node (pN2aM0)	Fibroplasia and melanophages in the dermis
3	48	M	Left foot	White papule with a subtle bluish coloration on one edge	8 months earlier 'present-for-years' growing black papule shaved off after minor trauma. Then regressive evolution	Left inguinal enlarged lymph node	Left inguinal nodes and lung (pN2aM1b)	Dermal fibroplasias, mild lymphocytic dermal infiltration melanophages, neoangiogenesis
4	36	M	Left side of the neck	Hypochromic macule with subtle blue hue on its upper border	2 years earlier onset of a black asymmetrical papule; 6 months earlier inflammatory reaction followed by the fading of the macule	Left cervical enlarged lymph node	Left cervical lymph node (pN2aM0)	Dermal fibroplasias, mild lymphocytic dermal infiltration few melanophages, neoangiogenesis
5	63	M	Left anterior abdomen (Fig. 2a)	3 cm in diameter white macule with erythematous edge. Associated paraneoplastic vitiligo	6 years earlier red nodule that progressively flattened and vanished	Left axillary enlarged lymph node	Left axillary lymph node (pN2aM0)	Dermal fibroplasia and neoangiogenesis
6	68	F	Left leg	Amelanotic macule, 10 × 15 mm	Pruritic erythematous pre-existing lesion 'for years'	Left inguinal enlarged lymph node	Left inguinal and iliac nodes and bone (pN2aM1c)	Dermal fibroplasias, neoangiogenesis, mild dermal lymphocytic infiltration
7	78	F	Left leg (Fig. 3a)	Pink angiomatoid macule (Fig. 3a)	6 months before diagnosis family noticed a red bleeding nodule that flattened and vanished	Left inguinal enlarged lymph node	Left inguinal nodes (pN2aM0)	Dermal fibroplasias, mild dermal lymphocytic infiltrate, melanophages and prominent neoangiogenesis

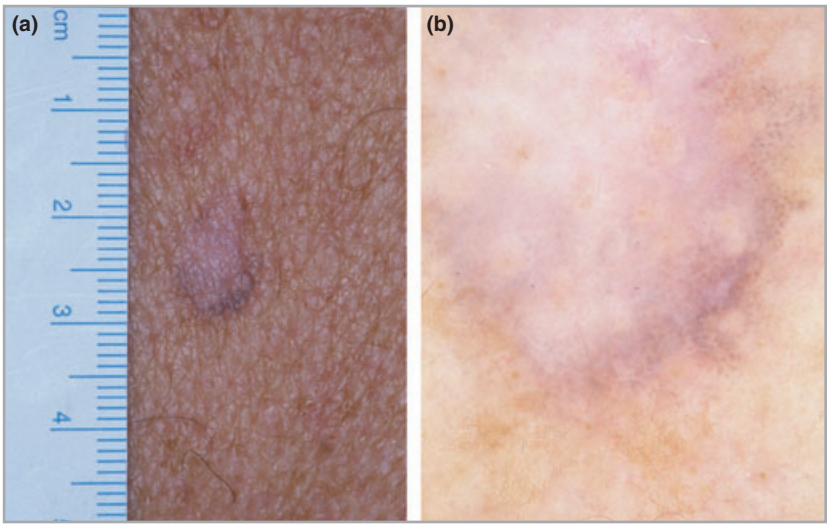

Fig 1. (a) Clinical and (b) dermoscopic images of patient 1. (b) Six of the seven criteria are present (the white transverse lighter bands are only observed with polarizing dermoscopy photo devices). Note the 'peppering' appearance in the lower part of the lesion. (Dermoscopy × 10, Heine Dermaphot, Herrsching, Germany.)

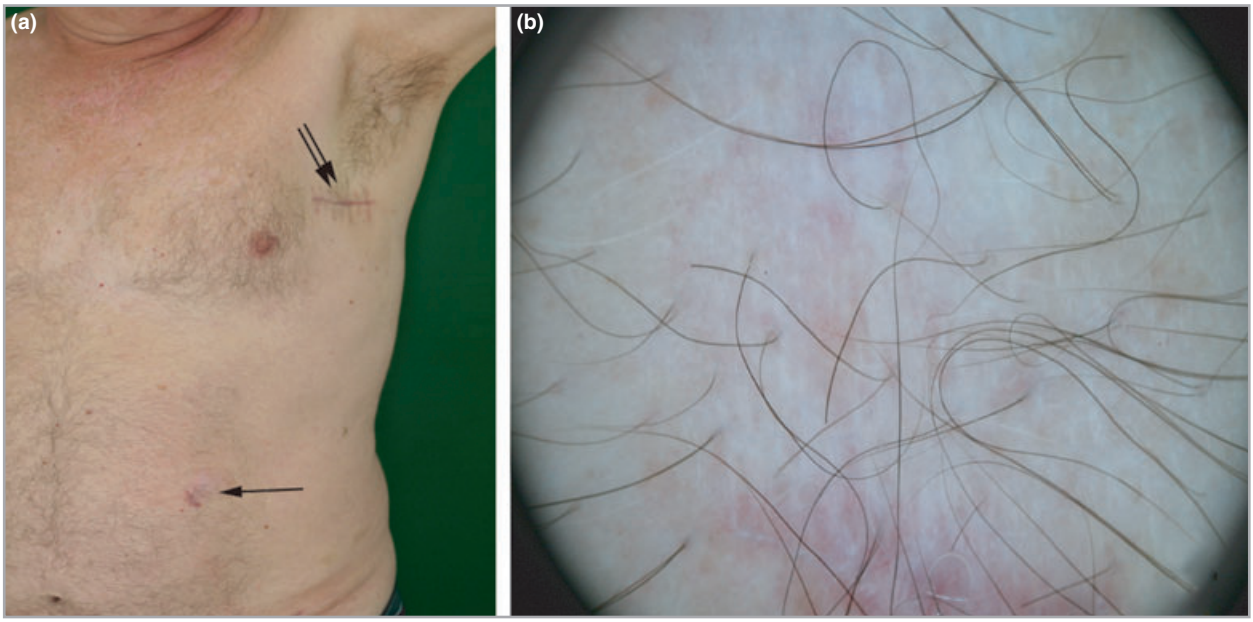

Fig 2. (a) Clinical and (b) dermoscopic images of patient 5. (a) Regressive primary lesion (arrow) and the scar of the metastatic lymph node surgical excision (double arrow). (b) Pink coloration of the background, white scar-like hypopigmentation and irregular vascular structures. Note the white transverse lighter bands demonstrated by the use of a polarizing light dermoscopy photo device. (Dermoscopy × 20, Dermlite Foto, 3 Gen, San Juan Capistrano, CA, U.S.A.)

correspond to the regressive primary lesion. Dermoscopic pictures were taken systematically with an adapted camera [Heine Dermaphot (Heine Optotechnik, Herrsching, Germany) or DermLite Foto (3Gen, San Juan Capistrano, CA, U.S.A.)]. When asked about the suspicious area (nonleading questions), five of the seven patients then recalled a past history of a preexisting tumour either pigmented or unpigmented with features of inflammation and, in several cases, with a history of bleeding after minimal trauma. Delay to prior medical examination ranged from 6 months to 6 years; no records of medical examination of the lesions when visible were available. In all five patients, the lesion healed spontaneously and left the observed scar which the patient then forgot about. Interestingly, in the two remaining patients the suspicious primary lesions were located on the back.

Histopathological analysis

For all patients, a histopathological analysis of the suspicious area was performed and the results are summarized in Table 1. Observed features were consistent with a fully regressive melanoma according to the criteria described by Smith and Stehlin[3] and later revised by High *et al.*[2] In summary, lesions exhibited thinning of the epidermis, scar-like fibrosis of the dermis,

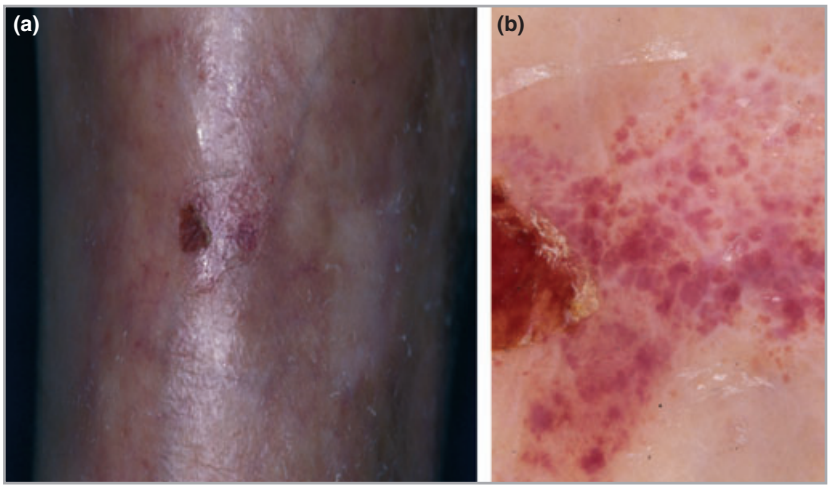

Fig 3. (a) Clinical and (b) dermoscopic images of patient 7. (b) Vascular pattern with pink coloration of the background, globular vessels and linear-irregular vessels. (Dermoscopy × 20, Dermlite Foto, 3 Gen, Vienna, Austria.)

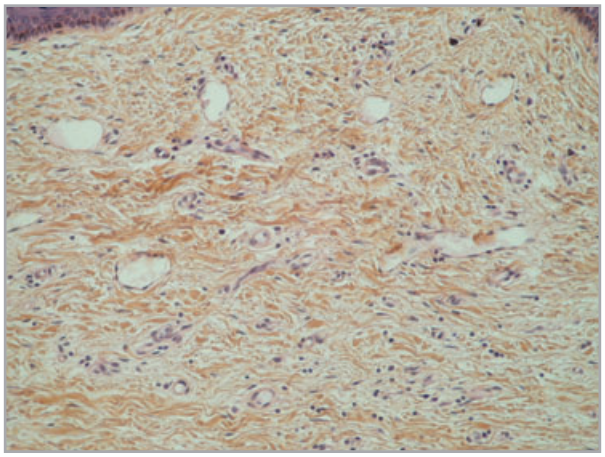

Fig 4. Histopathological features observed in patient 1 (haematoxylin and eosin–safran × 10). Note dermal fibroplasias, dilated vessels, few inflammatory cells and melanophages.

vascular hyperplasia and telangiectasias, mild lymphocytic infiltration and melanophages. However, no remaining malignant melanocytes were observed (Fig. 4).

Dermoscopic analysis

All suspicious lesions were examined with a handheld immersion dermoscope (Heine Delta 10 or Delta 20). A macroscopic as well as a dermoscopic picture of each lesion was taken and kept for further re-examination. Dermoscopic analysis of each lesion enabled recording of seven criteria: (i) white scar-like depigmented areas defined according to Zalaudek *et al.*[4] as a whitish discoloration lighter than the surrounding skin; (ii) grey-blue pepper-like granules defined by Zalaudek *et al.*[4] as thin grey-blue to black dust-like dots (these two features, usually associated with partial regression of primary melanoma, were also recorded by Massi *et al.* in 2001[5]); (iii) linear-irregular vessels, which are well known features of melanoma in the dermoscopy literature and have been included in the seven-point checklist by Argenziano *et al.*;[6] (iv) globular vascular structures – round-shaped pink to red dots (in our series these red globules varied in size from small dots, usually observed in melanocytic lesions, to much larger 0·5-mm lesions); (v) pink structureless coloration of the background either homogeneous or mixed with white scar-like areas observed in contrast with the surrounding skin; (vi) remnants of pigmentation, which are also a well-known dermoscopy feature of amelanotic melanoma – they could be observed either as structureless brown to grey-black macules often at the periphery of the lesion or as areas covered with a 'peppering' appearance; (vii) linear transverse white bands, only observed when using a polarizing light photodermoscopy system (DermLite) (they were not observed with a regular handheld immersion dermoscope or on pictures taken with an immersion nonpolarizing photosystem). This last feature has already been described by Agero *et al.*[7] in their work comparing dermatofibromas examined with either polarized or nonpolarized dermoscopy systems. It is thought to be due to the fibrosis of the dermis which is only observed with polarized illumination as this light offers better identification of dermal structures.

Statistical analysis

As we were dealing with an extremely rare phenomenon, only descriptive analysis was possible. Moreover, it is unlikely that further work will provide additional statistically evaluable data in the near future, and therefore we believe that the descriptive method was appropriate to investigate this phenomenon. Results are expressed as the percentage of patients in which a given criterion was present. These results are shown in Table 2.

Results

Our findings are summarized in Table 2. Among the seven recorded criteria, two were found in all cases: scar-like depigmentation and pink background coloration. Remnants of pigmentation and irregular-linear vessels are quite common

Table 2 Dermoscopic features

Dermoscopy features	Patients 1	2	3	4	5	6	7	Present (%)
Scar-like depigmentation	Y	Y	Y	Y	Y	Y	Y	100
'Peppering'	Y	Y	N	Y	N	N	N	43
Linear-irregular vessels	Y	N	Y	Y	Y	Y	Y	86
White transverse lighter bands	N	N	N	Y	Y	Y	N	43
Globular vessels	Y	Y	N	N	N	N	Y	43
Pink background	Y	Y	Y	Y	Y	Y	Y	100
Remnant of pigmentation	Y	Y	Y	Y	N	Y	Y	86

Y, observed criterion present; N, criterion absent.

features and were found in 86% of our patients. Peppering, one of the two dermoscopic presentations of the remnant of pigmentation, was observed in 43% of the cases; it is thought to correspond anatomically to the presence of melanophages.[4]

Discussion

According to several authors metastatic melanomas from unknown primary lesions represent 2–8% of all metastatic melanomas.[8–10] Two principal hypotheses are usually put forward to explain this phenomenon: either the primary lesion is located in a hidden anatomical site, almost always internal; or the primary lesion has undergone a regression, complete at the time of the diagnosis of the metastatic disease.[8] In our series, a search for mucosal or internal primary tumours was systematically performed but none were found.

Features of partial regression are found in 10–35% of primary melanoma cases.[1] However, cases of complete regression are much rarer. Only about 40 cases in the literature fulfil the histopathological criteria described by Smith and Stehlin;[3] 38 were reviewed by High *et al.*[2] The term 'fully regressed primary melanoma' only applies to histopathological findings, i.e. the complete absence of malignant melanocytes on serial sections. We report herein seven additional cases; their clinical and histopathological features are similar to previously reported observations.

Dermoscopy is a simple method for skin examination widely used in the diagnosis of cutaneous pigmented tumours. Its value in early and differential diagnosis of cutaneous melanoma has been clearly established by two independent meta-analyses and efficient diagnostic algorithms have been published.[11–13] The usefulness of dermoscopy in the diagnosis of the primary lesion in the case of metastatic melanoma associated with multiple atypical naevi has also been described.[14] However, to the best of our knowledge, there are only three reported cases of complete regression of melanoma in the dermoscopy literature. High *et al.*[2] report that dermoscopic examination of two of their 38 cases disclosed a dusty blue-grey coloration with 'peppering' images. The third case is quite unusual since it is the case of a patient who refused surgical treatment after clinical diagnosis of his melanoma and who was clinically and dermoscopically followed by Menzies and McCarthy for 4 years until complete regression of the lesion.[15] In this case the unique reported dermoscopy pattern after complete clinical regression was also 'peppering'.

Our series represents the first attempt of a systematic description of dermoscopy pattern associated with complete regression of the most probable primary lesion in cases of regional metastatic melanoma. The recorded features reflect vascular changes, colour changes and scarring phenomena. The observed features are not unusual as vascular structures (red globules and linear-irregular vessels) have already been described by Argenziano *et al.* in amelanotic or partially amelanotic melanomas.[6] Also, white scar-like depigmented areas and 'peppering' are part of the usual dermoscopic features of melanoma and are thought to be related to the regression process as shown by Zalaudek *et al.*,[4] and white transverse bright bands have been described in dermatofibromas and seem to be related to the dermal fibroplasias in these tumours as shown by Agero *et al.*[7] Concerning this last criterion, it is important to mention that it has only been observed with polarized light illumination devices in dermatofibromas as well as in the regressive melanomas described herein. The fact that all the features have already been described as associated with melanoma, either in cases of incomplete regression or in cases of an amelanotic primary tumour, reinforces the belief that the seven features of completely regressive melanoma described herein could be accurate.

On the basis of our work we believe that, in cases of metastatic melanoma of unknown origin, careful examination of the skin (especially in the draining area of a metastatic lymph node), should include dermoscopic examination of all suspicious areas, even in a case of extremely subtle changes. In the cases featuring the presence of white scar-like depigmentation (with transverse lighter bands seen with polarizing light), vascular changes or remnants of pigmentation (either macular or with a 'peppering' appearance), the diagnosis of a completely regressive primary melanoma should be considered and a biopsy taken, as this diagnosis should be based on clinical–pathological correlation.[16,17]

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