Dermoscopy of Solitary Angiokeratomas

A Morphological Study

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Objectives: To describe the dermoscopic structures and patterns associated with solitary angiokeratomas and to determine the sensitivity, specificity, positive predictive value, negative predictive value, and reproducibility of these dermoscopic features.

Design: Multicenter retrospective study.

Setting: University hospitals in Spain, Italy, Argentina, New York City, and Austria.

Patients: There were 256 patients total, and 32 specimens each of solitary angiokeratomas, melanocytic nevi, Spitz-Reed nevi, malignant melanomas, pigmented basal cell carcinomas, dermatofibromas, seborrheic keratoses, and other vascular lesions (19 angiomas, 7 pyogenic granulomas, 3 spider nevi, 2 lymphangiomas, and 1 venous lake) were consecutively collected from the laboratories of 8 hospitals. Diagnoses of all patients’ lesions were confirmed histopathologically.

Intervention: Dermoscopic examination.

Main Outcome Measures: The frequency, sensitivity, specificity, positive predictive value, negative predictive value, intraobserver agreement, and interobserver agreement of the different dermoscopic features associated with solitary angiokeratomas were calculated, and the differences were evaluated using the χ² or Fisher exact test.

Results: Six dermoscopic structures were evident in at least 50% of the solitary angiokeratomas: dark lacunae (94%), whitish veil (91%), erythema (69%), peripheral erythema (53%), red lacunae (53%), and hemorrhagic crusts (53%). Dark lacunae exhibited a sensitivity of 93.8% and a specificity of 99.1% (P < .001 for both), not being found in malignant melanomas or pigmented basal cell carcinomas. The positive predictive value was 93.8%, and the negative predictive value was 99.1%. The intraobserver agreement was perfect (κ, 1.00), and the interobserver agreement was excellent (κ range, 0.83-1.00) (P < .001 for both). Pattern 1, consisting of dark lacunae and whitish veil, exhibited a sensitivity of 84.4% and a specificity of 99.1% and was not found in malignant melanomas or pigmented basal cell carcinomas. The positive predictive value was 93.1%, the negative predictive value was 97.8%, the intraobserver agreement was perfect (κ range, 0.83-1.00) and the interobserver agreement was excellent (κ range, 0.83-1.00) (P < .001 for all).

Conclusion: Dermoscopy is helpful in improving the diagnostic accuracy of solitary angiokeratomas and allows the observer to differentiate them from other cutaneous tumors such as malignant melanomas and pigmented basal cell carcinomas.

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The term angiokeratoma was coined by Mibelli in 1889 and is derived from the 3 Greek words αγγειον, κερας, and ωμα, which mean “vessels,” “horn,” and “tumor,” respectively. Angiokeratomas are benign vascular lesions that histopathologically consist of dilated subpidermal vessels and, in most cases, are associated with an epidermal reaction that includes acanthosis or hyperkeratosis. They are seen clinically as solitary or multiple, red to black papules or plaques with a mamillated surface. The prevalence of angiokeratomas is estimated to be approximately 0.16% among the general population. Five clinical types are recognized, although there are reports describing other clinically atypical forms of angiokeratomas. These 5 clinical types are angiokeratoma of Mibelli (or angiokeratoma acroasphyti-cum digitorum), angiokeratoma of Fordyce (or angiokeratoma scroti), angiokeratoma corporis diffusum, angiokeratoma circumscriptum naeviforme, and solitary angiokeratoma, which is the lesion featured in this study.

Solitary angiokeratomas were first described by Imperial and Helwig in 1967.
They are the most common form of angiokeratomas, and the reported frequency varies from 70% to 83% of all angiokeratomas. Solitary angiokeratomas are seen clinically as a warty, keratotic, red-blue to black papule or nodule with a diameter of 2 to 10 mm. However, most lesions begin as bright, soft, nonkeratotic papules that grow larger and change to firm, blue-violaceous to black, keratotic papules. The clinical morphological structure and evolution of solitary angiokeratomas can be mistaken for others tumors. The most common differential diagnosis involves melanocytic nevi, Spitz-Reed nevi, malignant melanomas, pigmented basal cell carcinomas, seborrheic keratoses, dermatofibromas, and other vascular lesions such as hemangiomas or pyogenic granulomas.

Dermoscopy is a noninvasive in vivo technique that has revealed a new realm in the clinical morphological patterns of pigmented skin lesions. This technique allows for better visualization of structures within the epidermis, dermoepidermal junction, and superficial dermis. Previous studies demonstrated that the use of dermoscopy improves the clinical accuracy in diagnosing melanomas and other pigmented and vascular skin lesions and may help in differentiating benign from malignant lesions. The objectives of this study were to describe the dermoscopic characteristics of a series of solitary angiokeratomas and to investigate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPP), and reproducibility of dermoscopic structures and patterns associated with solitary angiokeratomas.

**METHODS**

Dermoscopic images of 32 histopathologically proven specimens of solitary angiokeratomas, collected at pigmented lesion clinics in Spain, Italy, Argentina, New York City, and Austria, were evaluated for the presence of dermoscopic features. Dermoscopic images of each lesion were obtained using a digital microscopy system (DermLite Foto; 3Gen, LLC, Dana Point, Calif) with a lens at 10-fold magnification (Dermaphot; Heine Optotechnik, Herrsching, Germany). Clinical data were obtained for each patient, including age, sex, and anatomical location of the specimen. A list of 37 dermoscopic criteria based on the conclusions of the Consensus Net Meeting on Dermoscopy, vascular structures described by Argenziano et al, and dermoscopic descriptions of solitary angiokeratomas by various authors were evaluated by one of us (P.Z.). These criteria and their frequency among solitary angiokeratomas are given in Table 1. The dermoscopic structures found in at least 50% of the cases were used to formulate global patterns that were most commonly found in our specimens of solitary angiokeratomas.

On the basis of these evaluations, we determined the diagnostic significance of different dermoscopic structures and patterns associated with solitary angiokeratomas. The criteria for calculating diagnostic values of each dermoscopic structure or pattern in solitary angiokeratomas were defined as follows: true-positive (TP) lesions were solitary angiokeratomas showing the dermoscopic structure or pattern being tested, true-negative (TN) lesions were nonsolitary angiokeratomas in which the dermoscopic structure or pattern was not detected, false-negative (FN) lesions were solitary angiokeratomas not showing the dermoscopic structure or pattern being tested, and false-positive (FP) lesions were nonsolitary angiokeratomas that revealed the dermoscopic structure or pattern. Sensitivity was the fraction of solitary angiokeratomas that revealed the dermoscopic structure or pattern under investigation among all solitary angiokeratomas and was calculated as TP/(TP + FN). Specificity was the fraction of lesions other than solitary angiokeratomas not showing the dermoscopic structure or pattern among all nonsolitary angiokeratomas and was calculated as TN/(TN + FP). The PPV was the fraction of solitary angiokeratoma lesions showing the dermoscopic structure or pattern among all lesions with that dermoscopic structure or pattern and was calculated as TP/(TP + FP). The NPV was the fraction of nonsolitary angiokeratoma lesions not showing the dermoscopic structure or pattern among all lesions without that dermoscopic structure or pattern and was calculated as TN/(TN + FN). Data analysis was performed using SPSS software version 10.0 (SPSS Inc, Chicago, Ill) for data management, giving 2 × 2 contingency tables, and the differences were calculated using the χ² or Fisher exact test.

All lesions in this study were evaluated for the presence of dermoscopic structures and patterns by one of us (P.Z.). The interobserver and intraobserver reproducibility was assessed for each dermoscopic structure and pattern evaluated for 35 lesions, which were randomly selected from 256 tumors included in the study. Regarding interobserver reproducibility, one of us (P.Z.) evaluated each structure and pattern and reevaluated them 3 months later. Regarding interobserver reproducibility, 2 of us (D.M.-R. and A.L.) evaluated the same lesions as those evaluated by P.Z., and the results were compared. Data analysis was performed using...
The study protocol was approved by the Local Research Ethics Committee of the Hospital Universitari de Sant Joan Faculty of Medicine, Reus, Spain. All participants gave oral informed consent.

Thirty-two solitary angiokeratomas were obtained. The lesions were obtained from 19 women (59%) and 13 men.

### Table 2. Frequencies of the Dermoscopic Structures and Patterns in Solitary Angiokeratomas and Other Cutaneous Tumors*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Red Lacunae</th>
<th>Dark Lacunae</th>
<th>Hemorrhagic Crusts</th>
<th>Whitish Veil</th>
<th>Erythema</th>
<th>Peripheral Erythema</th>
<th>Pattern 1</th>
<th>Pattern 2</th>
<th>Pattern 3</th>
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<tr>
<td>Solitary angiokeratomas</td>
<td>53</td>
<td>94</td>
<td>53</td>
<td>91</td>
<td>69</td>
<td>53</td>
<td>84</td>
<td>44</td>
<td>53</td>
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<tr>
<td>Malignant melanomas</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>75</td>
<td>41</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Basal cell carcinomas</td>
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<td>0</td>
<td>25</td>
<td>50</td>
<td>56</td>
<td>31</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
<td>9</td>
<td>31</td>
<td>16</td>
<td>10</td>
<td>0</td>
<td>0</td>
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<td>Dermatofibromas</td>
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<td>0</td>
<td>0</td>
<td>16</td>
<td>34</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Nevoid melanoma</td>
<td>0</td>
<td>0</td>
<td>16</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Spitz-Reed nevi</td>
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<td>0</td>
<td>0</td>
<td>22</td>
<td>22</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other vascular lesions</td>
<td>59</td>
<td>6</td>
<td>6</td>
<td>47</td>
<td>44</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

*Data are given as percentages.

SPSS software version 10.0, which calculated $k$ statistics with approximate significance. With regard to the interpretation of $k$ statistics, a value of 1.00 indicates perfect agreement, values greater than 0.80 are considered excellent, values between 0.61 and 0.80 are good, values between 0.40 and 0.60 are fair, and values less than 0.40 are poor.

Figure 1. Dermoscopic structures of solitary angiokeratomas, located on the left leg of a 28-year-old man (A), the right leg of a 27-year-old man (B), the trunk of a 55-year-old man (C), and the trunk of a 39-year-old woman (D). Dark lacunae (a) are sharply oval or round dark blue, dark violaceous, or black structures that correspond histopathologically to dilated vascular spaces located in the upper to middle dermis and that can be partially or completely thrombosed. Red lacunae (b) demonstrate the same dermoscopic feature as in (a) but are red or red-blue instead of black. Whitish veil (c) comprises an ill-defined structureless area with an overlying whitish “ground-glass” film that corresponds to hyperkeratosis and acanthosis. Hemorrhagic crusts (d) correspond to areas of bleeding. Peripheral erythema (e) manifests as a pinkish homogeneous area that could represent an inflamed lesion.
(41%) ranging in age from 15 to 84 years (median age, 49.6 years). Nineteen (59%) of 32 lesions were on the trunk, 9 (28%) were on the lower extremities, 3 (9%) were on the upper extremities, and 1 (3%) was on the face.

The following 6 dermoscopic structures were consistently seen in at least 50% of the solitary angiokeratomas (Table 2): dark lacunae (94%), whitish veil (91%), erythema (69%), peripheral erythema (53%), red lacunae (53%), and hemorrhagic crusts (53%) (Figures 1, 2, 3, 4, 5, and 6). When initially seen, none of the solitary angiokeratomas met the criteria for melanocytic lesions. However, 1 lesion showed a peripheral delicate pigment network similar to that seen in dermatofibromas (Figure 5). We evaluated the following 3 dermoscopic patterns: pattern 1 (dark lacunae and whitish veil), pattern 2 (dark lacunae, whitish veil, and peripheral erythema), and pattern 3 (dark lacunae, whitish veil, and hemorrhagic crusts) (Figure 7). Pattern 1 was present in 84% of solitary angiokeratomas, pattern 2 in 44%, and pattern 3 in 53% (Table 2). These patterns are not mutually exclusive.

Concerning other cutaneous tumors (Table 2), dark lacunae were observed in 6% of other vascular lesions, including 1 thrombosed angioma and 1 fibrosed angioma. They were not observed in any of the other tumors, including malignant melanomas and pigmented basal cell carcinomas. Whitish veil, erythema, and peripheral erythema were observed with relative frequency in other cutaneous tumors. Red lacunae were seen in 59% of other vascular lesions. Hemorrhagic crusts were observed in 25% of pigmented basal cell carcinomas, in 9% of seborrheic keratoses, and in 6% of other vascular lesions. Dermoscopic patterns 1 and 3 were observed in 6% and 3% of other vascular lesions, respectively. Pattern 2 was not observed in other cutaneous tumors.

Table 3 summarizes the results of the statistical analysis. These include the sensitivity, specificity, PPV, NPP, intraobserver agreement, and interobserver agreement (concordance between observers 1 and 2 and concordance between observers 1 and 3) for solitary angiokeratomas.

Dark lacunae exhibited a sensitivity of 93.8% and a specificity of 99.1%, with specificities of 100.0% compared with the 2 malignant tumors (malignant melanomas and pigmented basal cell carcinomas) (P < .001 for all) (Table 3). Dark lacunae showed a PPV of 93.8% and an NPV of 99.1% (P < .001 for both). Dark lacunae had perfect intraobserver agreement (κ, 1.00) and excellent to perfect interobserver agreement (κ range, 0.83-1.00) (P < .001 for both).

Figure 2. Pigmented skin lesion on the left leg of an 18-year-old woman. A, The clinical diagnosis was malignant melanoma. B, In the dermoscopic image, dark lacunae and whitish veil were observed. C, The histopathologic examination findings revealed a solitary angiokeratoma (hematoxylin-eosin, original magnification ×10).
Red lacunae showed a high specificity (91.5%) but a low sensitivity (53.1%) \( (P < 0.001 \text{ for both}) \), as they were frequently seen in other vascular lesions (Table 3). We observed a predominance of red lacunae in early solitary angiokeratomas (Figure 6). Red lacunae were not found in malignant melanomas or pigmented basal cell carcinomas. The NPV of red lacunae was 93.2\% \( (P < 0.001) \) (Table 3). The intraobserver agreement was perfect \( (κ, 1.00) \), and the interobserver agreement was excellent to perfect \( (κ \text{ range, } 0.80-1.00) \) \( (P < 0.001 \text{ for both}) \).

Whitish veil exhibited excellent sensitivity (90.6\%) but low specificity (63.4\%) \( (P < 0.001 \text{ for both}) \) (Table 3). Moreover, it was a common dermoscopic feature of malignant melanomas and pigmented basal cell carcinomas. The PPV was low (26.1\%), but the NPV was high (97.9\%) \( (P < 0.001 \text{ for both}) \). The intraobserver agreement was excellent \( (κ, 0.94) \), and the interobserver agreement was good \( (κ \text{ range, } 0.65-0.69) \) \( (P < 0.001 \text{ for both}) \).

The high specificity of hemorrhagic crusts (94.2\%) \( (P < 0.001) \) is noteworthy (Table 3). However, these were...
found in 25% of pigmented basal cell carcinomas and, in our experience, could be present in some malignant melanomas, although this was not reflected in the study. The high specificity of peripheral erythema (90.2%, P<.001) in the study was notable, although it was also observed in some malignant melanomas and pigmented basal cell carcinomas.

Pattern 1 exhibited a higher sensitivity (84.4%) compared with the other patterns, whereas pattern 2 showed a specificity of 100.0% (P<.001 for both) (Table 3). None of the 3 patterns seen in solitary angiokeratomas were found in malignant melanomas or pigmented basal cell carcinomas. Pattern 2 exhibited a PPV of 100.0%, and pattern 1 had the highest NPV (97.8%) (P<.001 for both). The intraobserver agreement for all 3 patterns was perfect (κ, 1.00), and the interobserver agreement was excellent to perfect for pattern 1 (κ range, 0.83-1.00) and good to excellent for the other patterns (κ range, 0.65-0.94) (P<.001 for all).

Dermoscopy is a noninvasive in vivo method for the diagnosis of pigmented and nonpigmented skin lesions. There has been extensive investigation in the realm of melanocytic lesions (especially malignant melanomas) and other pigmented skin lesions (such as pigmented basal cell carcinomas, seborrheic keratoses, dermatofibromas, or other vascular lesions such as hemangiomas or pyogenic granulomas). In the retrospective study by Imperial and Helwig, 3% of solitary angiokeratomas were correctly diagnosed by the examining physician. Furthermore, 15% of solitary angiokeratomas in the study by Imperial and Helwig and 20% of angiokeratomas in the study by Naranjo Sintes et al were diagnosed clinically as melanomas.

The results of this multicentric study reveal that 6 dermoscopic structures were evident in at least 50% of the solitary angiokeratomas and included dark lacunae, whitish veil, erythema, peripheral erythema, red lacunae, and hemorrhagic crusts. Red lacunae were defined as sharply ovoid or round red or red-blue structures that correspond histopathologically to wide and dilated vascular spaces located in the upper or middle dermis. Dark lacunae represent dilated vascular spaces in the upper dermis, and their dark violaceous, dark blue, or black color corresponds to vascular spaces that are partially or completely thrombosed. Whitish veil refers to an ill-defined structureless area with an overlying whitish "ground-
glass” film that corresponds to hyperkeratosis and acanthosis. Hemorrhagic crusts correspond to bleeding that can occur in some of these lesions. Finally, erythema and peripheral erythema are pinkish homogeneous areas that probably represent inflammation of the lesion and erythrocyte extravasation in the papillary dermis. At initial examination, none of the solitary angiokeratomas in this study met the dermoscopic criteria for melanocytic lesions. Only 1 of these lesions showed a peripheral delicate pigment network due to hyperpigmented rete ridges, which is akin to the network observed in dermatofibromas (Figure 5).

Dark lacunae are the most frequent dermoscopic finding in solitary angiokeratomas and represent the most valuable criterion for correctly diagnosing this vascular tumor. The sensitivity and specificity for dark lacunae were 93.8% and 99.1%, respectively (Table 3). Only 2 vascular lesions were initially seen with dark lacunae, 1 thrombosed angioma and 1 fibrosed long-standing angioma. No malignant melanomas or pigmented basal cell carcinomas were initially seen with dark lacunae, as they were seen only in other vascular lesions such as angiomas. We observed a predominance of red lacunae in early solitary angiokeratomas (Figure 6). Hemorrhagic crusts, erythema, and peripheral erythema showed low sensitivity and specificity, and they were commonly seen in malignant melanomas and pigmented basal cell carcinomas.

Pattern 1, consisting of dark lacunae and whitish veil, was determined to be the most consistent pattern observed in solitary angiokeratomas; however, the presence of dark lacunae alone was a better variable for diagnosing angiokeratomas. Pattern 1 exhibited a sensitivity of 84.4%, PPV of 93.1%, NPV of 97.8%, and specificity of 99.1% (Table 3). Pattern 1 showed excellent to perfect intraobserver and interobserver agreement. Pattern 2 (dark lacunae, whitish veil, and peripheral erythema) had a specificity of 100.0% for solitary angiokeratomas and exhibited a PPV of 100.0%.

In conclusion, the dermoscopic structures known as dark lacunae as well as pattern 1, consisting of dark lacunae and whitish veil, demonstrated high sensitivity, specificity, PPV, NPV, and reproducibility. The present study confirms that dermoscopy is a helpful tool that may increase the physician’s diagnostic accuracy of solitary angiokeratomas and allows the observer to differentiate them from other cutaneous tumors, including malignant melanomas and pigmented basal cell carcinomas.

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### Table 3. Diagnostic Significance and Reproducibility of Dermoscopic Structures and Patterns in Solitary Angiokeratomas

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positivity Predictive Value</th>
<th>Negative Predictive Value</th>
<th>$\kappa$ Intraobserver Agreement</th>
<th>$\kappa$ 1 Interobserver Agreement</th>
<th>$\kappa$ 2 Interobserver Agreement</th>
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<tr>
<td>Red lacunae</td>
<td>53.1</td>
<td>91.5</td>
<td>100.0</td>
<td>100.0</td>
<td>47.2</td>
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<td>1.00</td>
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<td>99.1</td>
<td>100.0</td>
<td>100.0</td>
<td>93.8</td>
<td>99.1</td>
<td>1.00</td>
</tr>
<tr>
<td>Hemorrhagic crusts</td>
<td>53.1</td>
<td>94.2</td>
<td>100.0</td>
<td>75.0†</td>
<td>56.7</td>
<td>93.4</td>
<td>1.00</td>
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<td>Whitish veil</td>
<td>90.6</td>
<td>63.4</td>
<td>25.0‡</td>
<td>50.0‡</td>
<td>26.1</td>
<td>97.9</td>
<td>0.94</td>
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<tr>
<td>Erythema</td>
<td>68.8</td>
<td>68.8</td>
<td>59.4†</td>
<td>43.8§</td>
<td>23.9</td>
<td>93.9</td>
<td>0.88</td>
</tr>
<tr>
<td>Peripheral erythema</td>
<td>53.1</td>
<td>90.2</td>
<td>93.8</td>
<td>68.8¶</td>
<td>43.6</td>
<td>93.1</td>
<td>1.00</td>
</tr>
<tr>
<td>Pattern 1</td>
<td>84.4</td>
<td>99.1</td>
<td>100.0</td>
<td>100.0</td>
<td>93.1</td>
<td>97.8</td>
<td>1.00</td>
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<tr>
<td>Pattern 2</td>
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<td>99.6</td>
<td>100.0</td>
<td>100.0</td>
<td>94.4</td>
<td>93.7</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Abbreviations: *1, between P.Z. and A.L.; ‡2, between P.Z. and D. M.-R.*

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REFERENCES


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