Dermoscopic Features of Skin Lesions in Patients With Mastocytosis

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**Objectives**: To evaluate dermoscopic features in a group of 127 patients with mastocytosis in the skin and to investigate the relationship between different dermoscopic patterns and other clinical and biological characteristics of the disease.

**Design**: Clinical and laboratory data were compared among patients with mastocytosis grouped according to the different dermoscopic patterns.

**Setting**: Patients were selected from the Instituto de Estudios de Mastocitosis de Castilla La Mancha and the Department of Dermatology of Hospital Universitario Ramón y Cajal from April 1 through September 30, 2009.

**Patients**: Overall, 127 consecutive patients (70 females [55.1%] and 57 males [44.9%]; median age, 17 years; range, 0-81 years) with mastocytosis in the skin were included in the study.

**Main Outcome Measures**: Evaluation of dermoscopic patterns and investigation of potential predictive factors for more symptomatic forms of the disease according to the need for daily antimediator therapy.

**Results**: Four distinct dermoscopic patterns were observed: yellow-orange blot, pigment network, reticular vascular pattern, and (most frequently) light-brown blot. A reticular vascular pattern was identified in all telangiectasia macularis eruptiva and some maculopapular mastocytosis. In turn, all patients with mastocytoma displayed the yellow-orange blot pattern. The reticular vascular dermoscopic pattern was associated with the need for daily antimediator therapy; this pattern, together with serum tryptase levels and plaque-type mastocytosis, represented the best combination of independent factors to predict the need for maintained antimediator therapy.

**Conclusions**: Dermoscopy is a feasible method for the subclassification of mastocytosis. Of note, a reticular vascular pattern is more frequently associated with the need for antimediator therapy.

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Dermoscopy is a noninvasive technique based on in vivo epiluminescence microscopy, which provides rapid and easy evaluation of the colors and microstructure of the epidermis, the dermoepidermal junction, and the papillary dermis, none of which are visible to the naked eye. In recent years, dermoscopy has emerged as a simple and useful tool for the diagnosis of melanocytic and nonmelanocytic skin lesions, and it has proven to be especially useful for early recognition of malignant melanoma. In this study, we report on the dermoscopic patterns of a large series (n = 127) of patients with mastocytosis and the relationship between those patterns and the clinical and biological characteristics of the disease.

METHODS

PATIENTS AND CLINICAL AND LABORATORY EXAMINATIONS

Overall, 127 consecutive patients (70 females [55.1%] and 57 males [44.9%]; median age, 17 years; range, 0-81 years) with MIS who were referred to the Instituto de Estudios de Mastocitosis de Castilla La Mancha or the Department of Dermatology of Hospital Ramón y Cajal from April 1 through September 30, 2009, were included in the study. Among the 127 patients, 61 (48.0%) were younger than 14 years and 66 (52.0%) were adults (median [range] age at the time of dermoscopy, 3 years [0-11 years] and 38 years [15-81 years], respectively). In all patients except those with mastocytoma who had typical clinical features at arrival, the diagnosis of MIS was established on the basis of a skin biopsy specimen. Median (range) time from disease onset to inclusion in the study was 11 years (3-60 years) in adults and 1 year (0-8 years) in children (P < .001). The study was approved by the local ethics committee, and all participants gave informed consent before entering the study, according to the tenets of the Declaration of Helsinki.

Classification of MIS was performed in all patients after careful examination of the skin following the criteria proposed by Hartmann and Henz (Table 1). Serum baseline tryptase (sBt) measurement was performed using a commercially available technique (CAP; Phadia AB, Uppsala, Sweden); clinical symptoms suggesting the release of MC mediators (eg, pruritus, flushing, abdominal cramping, diarrhea, nausea or vomiting, and anaphylaxis) also were recorded. The severity of mastocytosis-related symptoms was subsequently graded in 2 different subgroups according to the need for antimediator therapy (AMT) on a daily basis.

DERMOSCOPY

Mastocytosis skin lesions were examined by 2 independent dermatologists trained in dermoscopy (S.V.-G. and E.D.L.H.) using a DermLite instrument (3Gen LLC, Dana Point, California) at 10-fold magnification. No pressure was applied to avoid collapse of the capillaries. In those patients who displayed multiple skin lesions, 2 or more lesions were evaluated. According to the dermoscopic findings (eg, background color and the presence or absence of reticular lines or vessels), as many as 4 different dermoscopic patterns were identified, and each patient's lesions were classified into 1 of these 4 subgroups. Subsequently, the potential relationship between the dermoscopic patterns identified and specific clinical variants of the disease, sBt levels, and the severity of MC mediator symptoms was investigated.

TABLE 1. Classification of Cutaneous Mastocytosis by Hartmann and Henz

<table>
<thead>
<tr>
<th>Classification of Cutaneous Mastocytosis</th>
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<tbody>
<tr>
<td>1. Maculopapular cutaneous mastocytosis</td>
</tr>
<tr>
<td>2. Plaque-type cutaneous mastocytosis</td>
</tr>
<tr>
<td>3. Nodular cutaneous mastocytosis/mastocytoma (ie, solitary or multiple)</td>
</tr>
<tr>
<td>4. Diffuse cutaneous mastocytosis</td>
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<tr>
<td>5. Telangiectatic cutaneous mastocytosis</td>
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The interobserver and intraobserver reproducibility was assessed for each dermoscopic pattern evaluated for a lesion in all 127 patients. The evaluation of dermoscopic patterns was masked from clinical data. Digital dermoscopic images were obtained from all patients by 4 investigators (S.V.-G., I.A.-T., A.M., and L.E.), and the dermoscopic images were evaluated by 3 dermatologists (S.V.-G., E.D.L.H, and P.J.) who established the predominant dermoscopic pattern in each case. Regarding intraobserver reproducibility, 1 of the dermatologists (S.V.-G.) evaluated each lesion and reevaluated all of them 3 months later. Regarding interobserver reproducibility, 2 dermatologists (E.D.L.H and S.V.-G.) independently evaluated the same lesions, and the results were compared.

STATISTICAL ANALYSES

For all continuous variables, median and range were calculated but for categorical variables, frequencies were reported. The Mann-Whitney and χ² tests were used to assess the statistical significance of differences observed between groups for continuous and categorical variables, respectively. The χ² statistics were calculated to assess interobserver and intraobserver agreement. With regard to the interpretation of χ² 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. To identify the best combination of independent factors associated with each subgroup of patients, multivariate (ie, logistic regression) analysis was performed. For multivariate analyses, only those variables that showed statistically significant differences in the univariate study were included in the model. P ≤ .05 was considered statistically significant. For all statistical analyses, the SPSS 15.0 statistical software package (SPSS Inc, Chicago, Illinois) was used.

RESULTS

CLINICAL VARIANTS OF MIS

Overall, the different subtypes of MIS observed in the 127 patients studied were MPCM in 90 patients (70.9%), nodular mastocytosis (NM) in 11 patients (8.7%), solitary mastocytoma in 11 patients (8.7%), plaque-type mastocytosis (PM) in 8 patients (6.3%), and TMEP in 7 patients (5.5%). All patients except those with solitary mastocytoma displayed multiple skin lesions. Table 2
gives the distribution of the different clinical variants according to patient sex and age.

**DERMOSCOPIC FEATURES**

After careful examination of skin lesions, 4 dermoscopic patterns were identified (Figure 1) and named as follows: light-brown blot (51 patients [40.2%]), pigment network (41 patients [32.3%]), reticular vascular (18 patients [14.2%]), and yellow-orange blot (17 patients [13.4%]). In our study, the intraobserver and the interobserver agreement for the assignment of a dermoscopic pattern for each lesion were excellent (κ=0.87, P<.001, and κ=0.80, P<.001, respectively). Of note, in all patients who displayed multiple skin lesions, a predominant dermoscopic pattern was identified. The light-brown blot pattern was characterized by a light-brownish diffuse blot without any other identifiable features; pigment network lesions showed fine brown reticular lines, similar to those observed in some melanocytic lesions. In turn, lesions with a reticular vascular pattern consisted of thin reticular telangiectasias on a mild erythematous base with sparse vessels dotted throughout. Finally, yellow-orange blot lesions were characterized by a yellowish to orange faded color with an ill-defined margin. Of interest, the dermoscopic patterns observed for different skin lesions of the same patient were similar. The histologic correlation of each dermoscopic pattern is illustrated in Figure 2.

**Table 2. Number (Percentage) of Different Variants of Lesions in Patients With Mastocytosis in the Skin Grouped According to Age and Sex**

<table>
<thead>
<tr>
<th>Variant</th>
<th>Boys (n=38)</th>
<th>Girls (n=23)</th>
<th>Total (n=61)</th>
<th>Male (n=19)</th>
<th>Female (n=47)</th>
<th>Total (n=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPCM (n=90)</td>
<td>19 (54.3)</td>
<td>16 (45.7)</td>
<td>35 (100)</td>
<td>16 (29.1)</td>
<td>39 (70.9)</td>
<td>55 (100)</td>
</tr>
<tr>
<td>NM (n=11)</td>
<td>6 (60.0)</td>
<td>4 (40.0)</td>
<td>10 (100)</td>
<td>0</td>
<td>1 (100)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Solitary mastocytoma (n=11)</td>
<td>9 (81.8)</td>
<td>2 (18.2)</td>
<td>11 (100)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PM (n=8)</td>
<td>4 (80.0)</td>
<td>1 (20.0)</td>
<td>5 (100)</td>
<td>2 (66.7)</td>
<td>1 (33.3)</td>
<td>3 (100)</td>
</tr>
<tr>
<td>TMEP (n=7)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (14.3)</td>
<td>6 (85.7)</td>
<td>7 (100)</td>
</tr>
</tbody>
</table>

Abbreviations: MPCM, maculopapular cutaneous mastocytosis; NM, nodular mastocytosis; PM, plaque-type mastocytosis; TMEP, telangiectasia macularis eruptiva perstans.

**SERUM TRYPTASE**

The median (range) sBt level was 9 ng/mL (1-508 ng/mL) with significantly (P<.001) higher values in adults compared with children (median, 24.5 vs 6 ng/mL, respectively). Of interest, sBt levels were significantly higher in patients with a reticular vascular pattern vs those with the light-brown blot (P=.02), pigment network (P=.02), or yellow-orange blot profile (P<.001) (median, 24.5 vs 10 ng/mL, 9 ng/mL, and 5.4 ng/mL, respectively) (Figure 4A), with the level in those with the yellow-orange blot profile being significantly lower than in those with the light-brown blot (P=.02) and pigment network patterns (P=.04). Of note, all these differences lost their statistical significance when adult and pediatric patients were separately considered except for the higher sBt levels found among children with reticular vascular vs yellow-orange blot patterns (10.5 vs 5.2 ng/mL; P=.03).

Figure 4B shows differences in sBt levels between the distinct clinical forms of MIS. Of interest, sBt levels were significantly higher in the TMEP group (median, 84.9 ng/mL) vs all other groups except for the patients with PM (MPCM, 21.7 ng/mL [P=.001]; NM, 9.8 ng/mL [P=.003]; and solitary mastocytoma, 4.2 ng/mL [P<.001]). Conversely, sBt levels in patients with mastocytoma were significantly lower than those of the remaining disease groups (P=.001). When dividing all patients into adult or pediatric groups, differences in sBt levels were restricted to TMEP vs MPCM (84.9 vs 21.7 ng/mL; P=.009) and PM vs MPCM (288 vs 21.7 ng/mL; P=.005) in adults; however, in children, only patients with mastocytoma showed significantly lower sBt levels compared with all other groups except patients with PM.

**NEED FOR ANTIMEDIATOR THERAPY**

In 75 patients (59.1%), mastocytosis-related symptoms were mild or absent, and patients did not need AMT or only needed it on demand; conversely, in the remaining 52
Figure 1. Examples of the 4 different dermoscopic patterns identified in patients with mastocytosis in the skin. A, In a 9-year-old boy, maculopapular cutaneous mastocytosis with a light-brownish blot were observed on dermoscopy without any identifiable dermoscopic structure (ie, the characteristic light-brown blot pattern). B, In a 7-year-old boy, maculopapular cutaneous mastocytosis and a light-brown blot were observed on dermoscopy. C, In a 25-year-old woman, maculopapular cutaneous mastocytosis and fine brown reticular lines were observed on dermoscopy, typical of the pigment network pattern. D, In a 57-year-old man, maculopapular cutaneous mastocytosis and a pigment network pattern were observed on dermoscopy. E, In a 59-year-old woman, maculopapular cutaneous mastocytosis and thin reticular telangiectasias on a mild erythematous base with sparse vessels dotted throughout were observed on dermoscopy (ie, the reticular telangiectatic dermoscopic pattern). F, In a 46-year-old woman, telangiectatic mastocytosis and a reticular vascular dermoscopic pattern were observed on dermoscopy. G, In a 9-month-old boy, solitary mastocytoma manifesting as a yellowish to orange discoloration with an ill-defined margin was observed on dermoscopy (ie, the yellow-orange blot dermoscopic pattern). H, In a 4-month-old girl, solitary mastocytoma and a yellow-orange blot were observed on dermoscopy.
patients (40.9%), daily need for AMT was observed due to maintained symptoms. The percentage of patients who needed daily AMT was significantly higher among adults compared with children (51.5% vs 29.5%; \( P = .01 \)) and in

Figure 2. Histologic correlation with the 4 dermoscopic patterns (hematoxylin-eosin, original magnification \( \times 40 \)). A, The light-brown pattern showed mild and homogeneous hyperpigmentation of the basal layer associated with a dense dermal infiltrate of mast cells with scattered eosinophils. B, The pigmented network pattern correlated with a marked hyperpigmentation of the basal layer, more marked on the rete ridges, associated with a slight dermal infiltrate of mast cells. C, The main histopathologic feature of lesions with reticular vascular pattern was the dilation of the blood vessels. D, The yellow-orange blot pattern showed a dense infiltration of mast cells along the papillary and reticular dermis.
those patients with increased sBt levels of 10 ng/mL or greater compared with patients with sBt levels less than 10 ng/mL (66.7% vs 15.6%; \(P < .001\)) independent of the age group (65.3% vs 11.8% \(P < .001\) in adults and 71.4% vs 17.0% \(P < .001\) in children). Regarding the association between AMT and the clinical forms of the disease, patients with PM needed continuous AMT more frequently than all other groups (87.5% vs 37.8%; \(P = .008\)), but none of the patients with solitary mastocytoma (compared with 44.8% of all other clinical forms of MIS; \(P = .003\)) required AMT on a daily basis.

Regarding dermoscopic patterns (Table 4), the need for daily AMT was higher among patients with a reticular vascular pattern vs all other dermoscopic patterns (77.8% vs 34.9%; \(P = .001\)); in contrast, only 17.6% of patients with a yellow-orange blot pattern needed daily AMT (compared with 44.5% of patients with other dermoscopic patterns). Of note, of those 17 patients (11 with mastocytoma and 6 with NM) with a yellow-orange blot pattern, the patients with NM needed continuous AMT more frequently than patients with mastocytoma (50.0% vs 0%; \(P = .03\)). In contrast, no significant differences were observed in the daily need for AMT among the 18 patients with a reticular vascular pattern (81.8% of patients with MPCM compared with 71.4% of patients with TMEP; \(P > .99\)). However, when patients with MPCM were separately considered, a higher frequency of need for daily AMT was observed among those with a reticular vascular pattern vs other dermoscopic profiles (81.8% vs 32.9%; \(P = .003\)). In line with these findings, a reticular vascular pattern also was more frequently associated with daily need for AMT (compared with all other cases) when adults (78.6% vs 44.2%; \(P = .02\)) and children (75.0% vs 26.3%; \(P = .07\)) were separately considered.

In univariate analysis, the following variables were included: clinical form (ie, MPCM, PM, NM, TMEP, and mastocytoma), dermoscopic pattern (ie, light-brown blot, pigment network, reticular vascular, and yellow-orange pattern).
blot), sBt level, and age group (ie, adults and children). Multivariate analysis of predictive disease features for the need for daily AMT (Table 5) showed that the combination of sBt level (ie, >10 ng/mL), PM, and a reticular vascular pattern was the most informative independent factor; of note, no patients displayed all 3 factors simultaneously. On the basis of these results, a scoring system was built that proved to have high efficiency (positive predictive value, 0.9; 95% confidence interval [CI], 0.78-1.03; negative predictive value, 0.69; 0.60-0.78) to properly classify patients with MIS according to the need for AMT when at least 2 of those factors are simultaneously present (≥2 of 3). These results contrast with predictive values observed when 1 or more of those factors are present (score of ≥1 of 3) (positive predictive value, 0.65; 95% CI, 0.53-0.76; negative predictive value, 0.86; 0.78-0.95).

To our knowledge, only 1 study in a small series of patients with mastocytosis (ie, 3 patients with TMEP and 3 with UP) has been published so far,18 in which 2 different dermoscopic patterns were described (ie, a pigment network and a vascular pattern). Of interest, the 2 patterns reported in this study showed histologic correlation with UP and TMEP, respectively. Several years before, Arpaia et al19 had described the dermoscopic pattern of a solitary maculopapular mastocytosis lesion as a delicate pale pigmented network. We report on the largest series of dermoscopic patterns observed in mastocytosis described so far in the literature. Overall, 4 clearly distinguishable dermoscopic patterns were identified: light-brown blot, pigment network, reticular vascular, and yellow-orange blot.

The light-brown blot pattern was the most frequent dermoscopic pattern in our series. It accounted for a large proportion of all patients with MPCM and PM. Dermoscopic findings in these patients were similar to those observed in acral nevus20 and some actinic lentigos (S.V.-G. et al, unpublished data, January 2009).

In turn, dermoscopic features of patients with a pigment network pattern were consistent with previously reported data pertaining to mastocytosis, and they have been related to the potential accumulation of melanin in the basal layer of the epidermis due to proliferation of MC within the dermis.21 This pattern typically is seen in melanocytic lesions other than mastocytosis, such as dermatofibroma,22 solar lentigo,23 pigmented seborrheic keratoses,24 accessory nipple,25 Kaposi sarcoma,19 and even healthy skin.26 In our series, the pigment network pattern was present in approximately one-third of all patients with mastocytosis, with a slight predominance among those with MPCM and PM, similar to the light-brown blot pattern profile.

Thin telangiectasias detected in the reticular vascular pattern occur due to the presence of numerous proliferating vessels within the papillary dermis, which could reflect local release of MC-derived angiogenic factors.27 The vascular dermoscopic pattern has been previously described in clear cell acanthoma,28 nonpigmented eccrine poromas,29,30 squamous cell carcinoma,31 amelanotic melanoma,32 and porocarcinoma.32 Of interest, this pattern of thin telangiectasia is not seen commonly in these other conditions. In our series, a reticular vascular pattern, in which MCs are typically located around dilated capillaries of the superficial plexus of the upper dermis, was systematically found in patients with TMEP and in a small proportion of those with MPCM.

The yellow-orange blot dermoscopic pattern has been reported in a wide variety of skin lesions characterized by a xanthogranulomatous dermal infiltrate, which include juvenile xanthogranuloma,34 sebaceous hyperplasia,35,36 reticulohistiocytoma, xanthomatous dermatofi-
brom, and adult xanthogranuloma. Of interest, in our series, a similar yellow-orange blot pattern was systematically observed among children with mastocytoma and in approximately half of all patients with NM.

Also, a clear association between the subtype of MIS and these dermoscopic patterns is demonstrated. On the basis of these observations, a question remained regarding the potential effect of such patterns on the behavior of the disease and the severity of MY mediator release-associated symptoms. In this regard, our results clearly show that high sDBt levels (ie, >10 ng/mL), together with a PM and the presence of a reticular vascular dermoscopic pattern, are highly predictive of the daily need for AMT. Currently, it is well known that sDBt levels correlate with the overall MC burden; in fact, an sDBt level higher than 20 ng/mL is highly suggestive of systemic involvement in MIS, and it is 1 of the World Health Organization minor criteria for diagnosis of systemic mastocytosis. Furthermore, increased sDBt levels also have been associated with the severity of MY mediator release symptoms not only in mastocytosis but also in allergic diseases. In our study, sDBt levels were higher in adults compared with children, in accordance with a higher frequency of systemic involvement and a longer follow-up since the onset of the disease in adults. Nevertheless, higher sDBt levels were associated with a more frequent need for daily AMT in the adult and pediatric groups. In line with these findings, multivariate analysis showed that sDBt levels but not patient age proved to be a powerful independent predictive factor of the need for daily AMT, supporting the notion that tryptase levels by themselves are a powerful predictive factor of a more symptomatic disease.

In line with previous observations, all patients with TMEP in our series showed a reticular vascular dermoscopic pattern. However, this pattern also was detected in some patients with MPCM; of interest, these latter patients more frequently required daily AMT than other patients with MPCM. Overall, the presence of a reticular vascular pattern was associated with an increased need for daily AMT; on the basis of these findings, it could be hypothesized that in combination with other variables, dermoscopy could provide additional help in the identification of patients at risk for more severe symptoms, independently of tryptase levels or the clinical subtype of MIS, as confirmed in our study by multivariate analysis. Another disease feature that proved to be associated with more severe symptoms was the clinical form of MIS; PM was associated with a higher proportion of patients receiving daily AMT, but solitary mastocytoma was less symptomatic, with no patients needing daily AMT. At least in adults, this could occur due to a higher MC burden, as supported by the extremely higher sDBt levels observed within this group of patients.

A limitation of our study is that patients previously diagnosed as having mastocytosis were evaluated. A future prospective study including dermoscopy evaluation at the time of disease diagnosis may clarify whether dermoscopy may predict better evaluation in the future.

The results of this study reveal that 4 dermoscopic patterns were evident in MIS, which can be easily evaluated in the diagnostic workup of cutaneous mastocytosis. However, these patterns are not totally specific for MIS, so the diagnosis needs to be confirmed by the results of a skin biopsy in most cases. The dermoscopic patterns, in combination with sDBt levels and the clinical forms of MIS, also provide useful information for the identification of more symptomatic forms of the disease that will require daily AMT. Strict and prospective follow-up of patients can allow the possibility of detecting changes in dermoscopic patterns throughout the evolution of the disease (ie, children with a progressive decrease in skin lesions) or for the follow-up of response of skin lesions to different therapies, such as psoralen–UV-A, cytoxic, or targeted therapies.

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