The Significance of Eccentric and Central Hyperpigmentation, Multifocal Hyper/hypopigmentation, and the Multicomponent Pattern in Melanocytic Lesions Lacking Specific Dermoscopic Features of Melanoma

Alda Arevalo, MD; Davide Altamura, MD; Michelle Avramidis, BSc; Andreas Blum, MD; Scott Menzies, MBBS, PhD

Objective: To examine the significance of eccentric hyperpigmentation (EH), central hyperpigmentation (CH), multifocal hyper/hypopigmentation (MH/HP), and the multicomponent pattern (MCP) in melanocytic lesions lacking specific dermoscopic features of melanoma.

Design: A total of 3367 benign and malignant melanocytic lesions (n=341 melanomas, excluding lentigo maligna and lentigo maligna melanoma) were examined to identify those lesions lacking specific dermoscopic features of melanoma but having any of the global patterns of EH, CH, MH/HP, and MCP.

Setting: Dermoscopic images were collected from lesions excised or undergoing sequential digital monitoring from the Sydney Melanoma Diagnostic Centre, a tertiary referral institution located in Sydney, Australia.

Main Outcome Measure: The odds ratio (OR) for melanoma of EH, CH, MH/HP, and MCP.

Results: While EH (OR, 3.3; 95% confidence interval [CI], 2.5-4.6) and MCP (OR, 15.4; 95% CI, 11.9-19.9) were significant predictors of melanoma when total melanomas vs nevi were analyzed, there was no significant difference between the frequency of any of the global patterns in melanomas vs benign nevi lacking specific dermoscopic features of melanoma.

Conclusion: Based on our study results and previous prevalence data on these global patterns in benign nevi, we do not believe that lesions with EH or MCP require closer observation than other benign nevi lacking specific dermoscopic features of melanoma.

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A typical (Clark, dysplastic) and banal acquired nevi have previously been classified according to global structural features found on dermoscopy.1,2 Such features include reticular, globular, or homogeneous patterns with combinations of those types: eccentric hyperpigmentation (EH), central hyperpigmentation (CH), and multifocal hyper/hypopigmentation (MH/HP). In a follow-up study of both benign and malignant melanocytic lesions by Blum et al.3 certain global patterns were found more frequently in melanoma. In particular, the multicomponent pattern (MCP) with all 3 reticular, globular, and homogeneous structures had an odds ratio (OR) of 12.5 for melanoma, 2.9 for EH, and 2.2 for MH/HP. Such observations have been recently reproduced by others.4

Because of these observations, EH, MH/HP, and MCP have been considered indications for close monitoring or excision of nevi. However, to date, no study (to our knowledge) has examined these patterns in melanocytic lesions that have none of the more specific dermoscopic features of melanoma. With this in mind, we examined a large series of sequential dermoscopic images of melanocytic lesions with these global patterns but without other specific dermoscopic features of melanoma. The aim was to define which global patterns may predict melanoma in nevi that show no dermoscopic features of melanoma.

METHODS

Dermoscopic images of 3367 melanocytic lesions, excluding lentigo maligna and lentigo maligna melanoma (n=341 melanomas), imaged at the Sydney Melanoma Unit (Sydney Melanoma Diagnostic Centre, Sydney, Australia) since 1991 were examined by 2 observers (A.A. and D.A.). The images were obtained using a dermoscopic camera (Dermaphot; Heine Ltd, Herrsching, Germany) or a digital imaging device (So-
The frequency of the global dermoscopic patterns of all melanomas was compared with those of benign melanocytic lesions, true EH (OR, 3.3) and the MCP (OR, 15.4) were significant predictors of melanoma (Table 1). However, 92% (n = 315) of melanomas and 28% (n = 846) of benign melanocytic lesions had specific dermoscopic features of melanoma (positive Menzies score). When all lesions without specific dermoscopic features of melanoma (negative Menzies score) were examined, there was no significant difference in any of the global patterns between the dermoscopically featureless melanomas (n = 26) and the benign melanocytic lesions (Table 2).

A number of investigators have reported that the global features of EH and MH/HP occur in benign nevi. In the original study by Hofmann-Wellenhof et al,1 who examined 829 atypical nevi in 23 individuals, 7.6% of the lesions had EH and 29% had MH/HP. None had MCP. Bologna et al,12 using nondermoscopic naked-eye examination found that only 3 of 59 nevi (5%) with EH (black dots) were melanoma arising within a nevus. It is unknown whether the 3 melanomas had dermoscopic features of melanoma. Pizzichetta et al13 described a small series of childhood nevi with EH, with some losing the feature over time. Zalaudek et al2 examined 1268 nevi in a wide age-selected population of 50 individuals and showed that 5% had EH, with no age trend, and 19% had MH/HP, which were less common in individuals younger than 31 years. In a more recent, larger study in which skin type and global nevus patterns of consecutive white-skinned patients in pigmentated lesion clinics were analyzed, similar results were seen, with 3.1% of nevi having EH, 19.3% having MH/HP, and 20.7% having CH.14

Two studies have examined these global patterns both in benign melanocytic lesions and in melanomas. In the original study by Blum et al,3 30% of the 234 lesions ex-
examined were melanomas. In that study, EH was a significant predictor of melanoma, with an OR of 2.9, which was consistent with our results (OR, 3.3). Their observation that an MCP was a highly significant feature of melanoma was also consistent with our findings (OR, 13 in their study vs OR, 15 in our study). They did not report whether any of the melanomas lacked the specific dermoscopic features of melanoma. In contrast to our study findings, MH/HP was also seen to be a less, but still significant predictor of melanoma (OR, 2.2). The low frequency of this pigmentation in both nevi and melanomas that we observed may be attributable to a more stringent definition.
Monitoring over a 3-month period.\textsuperscript{5,6} Such lesions are usually featureless. In our clinic, these are detected most accurately using the Menzies method, as in our study. Some of these lesions may lack any features of melanoma using the Menzies method, as in our study. However, it is unknown whether these had any features of melanoma using the Menzies method.\\n
In contrast to our results, 5 of 7 false-negative melanomas (dermoscopically featureless on pattern analysis) in our study were correctly identified as melanomas. They found that, for the diagnosis of melanoma, EH had an OR of 2.8, MH/HP had an OR of 1.5, and MCP had an OR of 11 (ORs derived from the tabled data). In contrast to our results, 5 of 7 false-negative melanomas (dermoscopically featureless on pattern analysis) that lack specific dermoscopic features of melanoma in our study are significantly different using \( \chi^2 \) analysis (or Fisher exact test when relevant), the odds ratio for the diagnosis of melanoma was calculated.

Twenty-six melanomas in our series were dermoscopically featureless. In our clinic, these are detected most frequently by the use of short-term digital dermoscopy monitoring over a 3-month period.\textsuperscript{5,9,10} Such lesions are usually mild to atypical with symmetrical or near symmetrical pigmentation pattern and little architectural disorder with no specific dermoscopic features of melanoma but with a patient history of change. More atypical lesions with greater architectural disorder and without a patient history of change also undergo short-term monitoring. Such lesions are never nodular or significantly raised. Featureless melanomas are also detected by long-term digital monitoring over standard surveillance periods (in our hands, usually after short-term monitoring) or with change detected by baseline total-body photography in patients with multiple dysplastic nevi.

Our results confirmed the above-mentioned findings that EH and the MCP are significant predictors of melanoma. However, 92% of the total melanomas in our study had specific dermoscopic features of melanoma and could be diagnosed without reference to these global patterns. Because of the high prevalence of these global patterns in nevi, we wanted to find out whether any of the patterns could be used to differentiate melanomas from nevi among melanocytic lesions that lack specific dermoscopic features of melanoma. In this regard, there was no difference between the frequency of EH, MCP, or any other global pattern in melanomas vs benign nevi among such lesions. Indeed, all 51 lesions that had true EH (and 35 more with pseudo-EH) without other specific features of melanoma were benign. While the MCP is a highly significant feature of melanoma overall (OR, 15), only 2 featureless melanomas had the MCP, and there was no difference in the proportion of benign nevi that had this feature. For this reason, we do not believe that such lesions require closer observation than other benign nevi that lack specific dermoscopic features of melanoma on morphological grounds alone.

Table 1. Frequency of Global Dermoscopic Patterns in 341 Melanomas and 3026 Benign Melanocytic Lesions

<table>
<thead>
<tr>
<th>Global Pattern</th>
<th>No. (%)</th>
<th>Odds Ratio (95% Confidence Interval)\textsuperscript{a}</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>True eccentric</td>
<td>63 (18.5)</td>
<td>192 (6.3)</td>
<td>3.3 (2.5-4.6)</td>
</tr>
<tr>
<td>Pseudo-eccentric</td>
<td>6 (1.7)</td>
<td>61 (2.0)</td>
<td>...</td>
</tr>
<tr>
<td>Central</td>
<td>5 (1.5)</td>
<td>90 (3.0)</td>
<td>...</td>
</tr>
<tr>
<td>Hyper/hypopigmentation</td>
<td>0</td>
<td>17 (0.5)</td>
<td>...</td>
</tr>
<tr>
<td>Multicomponent</td>
<td>174 (51)</td>
<td>470 (15.5)</td>
<td>15.4 (11.9-19.9)</td>
</tr>
<tr>
<td>No pattern</td>
<td>129 (37.8)</td>
<td>2297 (75.9)</td>
<td>0.19 (0.15-0.24)</td>
</tr>
</tbody>
</table>

\textsuperscript{a}When a global pattern was significantly different using \( \chi^2 \) analysis (or Fisher exact test when relevant), the odds ratio for the diagnosis of melanoma was calculated.

Table 2. Frequency of Global Patterns in 26 Melanomas and 2180 Benign Melanocytic Lesions Lacking Specific Dermoscopic Features of Melanoma\textsuperscript{a}

<table>
<thead>
<tr>
<th>Global Pattern</th>
<th>No. (%)</th>
<th>Benign Melanocytic Lesions</th>
<th>( P ) Value\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>True eccentric</td>
<td>0</td>
<td>51 (2.3)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Pseudo-eccentric</td>
<td>0</td>
<td>35 (1.6)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Central</td>
<td>1 (3.8)</td>
<td>55 (2.5)</td>
<td>.50</td>
</tr>
<tr>
<td>Hyper/hypopigmentation</td>
<td>0</td>
<td>8 (0.4)</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Multicomponent</td>
<td>2 (7.7)</td>
<td>141 (6.5)</td>
<td>.68</td>
</tr>
<tr>
<td>No pattern</td>
<td>23 (88.5)</td>
<td>1916 (79.9)</td>
<td>&gt;.99</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Negative Menzies score.

\textsuperscript{b}There was no significant difference in any of the global patterns between melanomas and benign melanocytic lesions (2-sided Fisher exact test).

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Correspondence: Scott Menzies, MBBS, PhD, Faculty of Medicine, University of Sydney, Sydney Melanoma Diagnostic Centre, Sydney Cancer Centre, Royal Prince Alfred Hospital, Camperdown, NSW 2050, Australia (scott.menzies@sswahs.nsw.gov.au).

Author Contributions: Dr Menzies had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Arevalo, Altamura, Avramidis, and Menzies. Acquisition of data: Arevalo, Altamura, Avramidis, and Menzies. Analysis and interpretation of data: Menzies. Drafting of the manuscript: Menzies. Critical revision of the manuscript for important intellectual content: Arevalo, Altamura, Avramidis, and Blum. Statistical analysis: Menzies. Obtained funding: Menzies. Administrative, technical, and material support: Menzies. Study supervision: Menzies.

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REFERENCES


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