Histopathological features of acquired dermal melanocytosis

Acquired dermal melanocytosis (ADM) is the term used for pigmentary disorders characterized by blue brown macules, most frequently seen on the face (acquired bilateral nevus of Ota-like macules, ABNOM), and rarely found on the trunk or extremities. Although extrafacial ADM and ABNOM are not usually considered separate entities because of similar features, there has been debate as to whether extrafacial ADM and ABNOM might be part of the same disease spectrum, with or without the same pathogenesis. In order to investigate the relationship between these two entities, the histopathological features of extrafacial ADM and ABNOM were evaluated. We examined nine cases of extrafacial ADM and ten cases of ABNOM. Biopsies were performed on both normal and lesional skin, or on lesional skin only. The sections were stained using hematoxylin-eosin, Fontana-Masson, and NKI/beteb. There was no difference in the degree of melanin pigmentation and the number of melanocytes per unit area in the lesional skin of the epidermis and dermis in the comparisons between extrafacial ADM and ABNOM. The mean depth of the dermal melanocytes was significantly increased in extrafacial ADM (0.88 ± 0.19 mm) compared to ABNOM (0.58 ± 0.19 mm); however, in both extrafacial ADM and ABNOM, dermal melanocytes were distributed from the upper to the mid dermis. In conclusion, there was no significant difference in the histopathological features, including relative depth of melanocytes, between extrafacial ADM and ABNOM. To the best of our knowledge, this is the first study to demonstrate by histopathology that extrafacial ADM is the same as ABNOM.

Key words: acquired dermal melanocytosis, acquired bilateral nevus of Ota-like macules, histopathology

Materials and methods

We examined nine patients with extrafacial ADM (7 females and 2 males) and 10 patients with ABNOM (9 females and 1 male). Informed consent was obtained from each patient before the diagnostic skin biopsy. The clinical features of extrafacial ADM are shown in Table 1 and Figure 1. Punch biopsies (2 mm) from skin lesions and perilesional normal skin were performed. However, in four cases of extrafacial ADM, biopsies from single skin lesions were performed. Melanin pigments were visualized with the Fontana-Masson staining, and melanocytes were detected by the NKI/beteb stain (Monosan, Uden, The Netherlands). The number of melanocytes as well as the amount of melanin pigment per unit area in the epidermis and dermis were evaluated, using image analysis software (Image Pro Plus Version 4.5). The image analysis was performed under constant magnification (original magnification ×100). For the measurement of melanin pigment, the ratio of pigmented area to measured epidermal (PA/EA) and dermal (PA/DA) area were evaluated in the lesional and perilesional normal skin. The number of melanocytes per measured epidermal (MC/EA) and derma area (MC/DA) were also evaluated to measure the quantity of
melanocytes in the lesional and perilesional normal skin. In addition to MC/EA, the number of melanocytes per certain length (1 mm) of the rete ridge (MC/1R) was also evaluated to investigate the number of epidermal melanocytes. The depth of the melanocytes was assessed by measuring from the top of the stratum granulosum to the deepest dermal melanocyte. The data from the individual groups were evaluated with the *t*-test.

**Results**

The ratio of PA/EA in the lesional skin was increased in both extrafacial ADM and ABNOM compared to the normal skin; however, these differences were not statistically significant (table 2). The PA/EA of lesional skin relative to the PA/EA of normal skin was similar in comparisons between the cases with extrafacial ADM (1.25) and the cases with ABNOM (1.51).

The PA/DA was significantly increased in the lesional skin of both the extrafacial ADM and the ABNOM compared to the perilesional normal skin. However, there was no difference between extrafacial ADM and ABNOM in the PA/DA of lesional skin.

Regarding the number of dermal melanocytes in ABNOM and extrafacial ADM, lesional skin had increased melanocyte counts compared to normal skin (table 3). On the other hand, ADM (both ABNOM and extrafacial ADM) appeared to have only a slightly increased pigmentation per unit area and number of the melanocytes in the epidermis. Considering the results of our previous study [9], the amounts of increased PA/EA, MC/EA and MC/1R in lesional skin were not as significant as for melasma.

The mean depth of dermal melanocytes was significantly increased in cases with extrafacial ADM (0.88 ± 0.19 mm) compared to ABNOM (0.58 ± 0.19 mm) (figure 2). To standardize the depth of the melanocytes, each value was divided

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**Table 1. Clinical features of extrafacial ADM**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Duration (years)</th>
<th>Color</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>18</td>
<td>0.3</td>
<td>Brown</td>
<td>Right dorsum of hand</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>69</td>
<td>7</td>
<td>Brown</td>
<td>Both dorsum of feet</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>64</td>
<td>20</td>
<td>Gray blue</td>
<td>Upper back</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>32</td>
<td>20</td>
<td>Brown</td>
<td>Left dorsum of foot</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>14</td>
<td>3</td>
<td>Gray blue</td>
<td>Right palm</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>16</td>
<td>1</td>
<td>Gray blue</td>
<td>Left palm</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>62</td>
<td>0.3</td>
<td>Brown blue</td>
<td>Face, both dorsum of hands</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>47</td>
<td>10</td>
<td>Brown blue</td>
<td>Left dorsum of hand</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>35</td>
<td>20</td>
<td>Brown blue</td>
<td>Right dorsum of hand</td>
</tr>
</tbody>
</table>

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**Figure 1.** The clinical photos of extrafacial ADM. Brown pigmented macules and patches were on the dorsum of the right hand in patient 9 (A) and dorsum of left foot of patient 4 (B).

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**Table 2. Quantitative analysis of melanin pigment in extrafacial ADM and ABNOM**

<table>
<thead>
<tr>
<th></th>
<th>Extrafacial ADM</th>
<th>ABNOM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Lesion</td>
</tr>
<tr>
<td>PA/EA</td>
<td>10.01 ± 7.33</td>
<td>15.13 ± 13.61</td>
</tr>
<tr>
<td>PA/DA</td>
<td>0.06 ± 0.14</td>
<td>0.80 ± 0.54*</td>
</tr>
</tbody>
</table>

PA/EA: The ratio of pigmented area to measured epidermal area (%); PA/DA: The ratio of pigmented area to measured dermal area (%); * p < 0.05.
by the measured depth of the dermis. Then, there was no significant difference between extrafacial ADM and ABNOM in the relative depth of the melanocytes (table 4).

Table 3. Quantitative analysis of the number of melanocytes in extrafacial ADM and ABNOM

<table>
<thead>
<tr>
<th></th>
<th>Extrafacial ADM</th>
<th>ABNOM</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC/EA</td>
<td>46.28 ± 34.79</td>
<td>46.02 ± 48.10</td>
</tr>
<tr>
<td>MC/1R</td>
<td>5.38 ± 3.38</td>
<td>6.00 ± 3.82</td>
</tr>
<tr>
<td>MC/DA</td>
<td>0.40 ± 0.68</td>
<td>20.10 ± 16.92*</td>
</tr>
</tbody>
</table>

MC/EA: Number of melanocytes per measured epidermal area (mm²); MC/1R: Number of melanocytes per 1-mm length of rete ridge; MC/DA: Number of melanocytes per measured dermal area (mm²); * p < 0.05.

Table 4. Quantitative analysis of the number of melanocytes in extrafacial ADM and ABNOM

<table>
<thead>
<tr>
<th></th>
<th>Extrafacial ADM</th>
<th>ABNOM</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean depth</td>
<td>0.88 ± 0.19</td>
<td>0.58 ± 0.20</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Relative depth</td>
<td>0.46</td>
<td>0.44</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Mean depth: The mean depth of dermal melanocytes was assessed by measuring from the top of the stratum granulosum to the deepest dermal melanocyte (mm); Relative depth: The relative depth of dermal melanocyte was estimated by the ratio of mean depth of dermal melanocytes to measured depth of dermis (from the top of the granular layer to the deep dermis).

Discussion

ADM is commonly found on the face; mainly the lateral sites of the forehead, temples, upper eyelids, malar areas and root of the nose [1]. However, it rarely occurs on the central area of the face, which should be differentiated from centrofacial melasma [10]. Mataix et al. [11] classified ADM into two groups, facial and extrafacial variants, and reported that extrafacial ADM demonstrated a predilection for men and had a late age of onset. Interestingly, in our study, both extrafacial ADM and ABNOM demonstrated a predilection for women and had a middle age onset; however, these findings are limited by the small sample size studied. In addition, there was no significant difference in the number of melanocytes and the amount of melanin pigment per unit area between ABNOM and extrafacial ADM. The dermal melanocytes of extrafacial ADM were deeper than in cases with ABNOM; however, the relative depth confirmed that the dermal melanocytes were distributed from the upper to the mid dermis in both extrafacial ADM and ABNOM. These results support the suggestion that ABNOM and extrafacial ADM have a similar histopathology [4].

There have been some cases (including our patient 7) where ADM simultaneously involved the face bilaterally and both extremities [12-14]. It has been suggested that these “bilateral” extrafacial ADM cases may not be a separate entity from ABNOM [5]. However, extrafacial ADM often has unilateral involvement, and it is doubtful that the “unilateral” extrafacial ADM cases have the same pathogenesis as ABNOM. A few cases of ADM involving only unilateral extremities have been reported and in some of these cases there was an association with previous trauma, sun exposure, or pregnancy [6-8, 14]. However, in our histopathological evaluation, six of the nine cases of extrafacial ADM had unilateral involvement of the extremities and were not different from the ABNOM cases.

The small number of patients was the most important limitation of our study. In addition, the entire lesion and
the continuous changes of pigmentation or number of melanocytes from lesional (pigmented) to perilesional normal (non-pigmented) skin were not available for histopathological analysis.

In conclusion, despite the limitations of our small sample size, these findings suggest that there is no significant difference in the histopathological features, including the degree of melanin pigmentation, number of melanocytes, and relative depth of melanocytes, between extrafacial ADM and ABNOM. This is the first study to demonstrate that extrafacial ADM has the same histopathology as ABNOM. Further studies are needed to identify the significant factors involved in determining the site and distribution of ADM.


References