Letter to the Editor

Merkel cell carcinoma in situ associated with actinic keratosis: fortuitous or serendipitous?

To the Editor,

Merkel cell carcinoma (MCC) commonly presents as a malignancy confined to the dermis. Fewer than 10% of cases show varying degrees of epidermal involvement.1 Only a small number of cases of entirely intraepidermal ‘in situ’ MCC (MCCIS) have been reported.2–8 All but one7 of these cases were encountered as an incidental histopathological finding in the presence of an otherwise common cutaneous lesion, such as squamous cell carcinoma in situ,2–5 trichilemmal cyst6 or seborrheic keratosis.8

Figure 1A illustrates a gritty, indurated plaque above the upper lip in a 68-year-old woman, skin-type I, who was followed regularly because of a history of multiple actinic keratoses and basal cell carcinomas. The clinical differential diagnosis included actinic keratosis and squamous cell carcinoma. A shave biopsy specimen disclosed rare intraepidermal nests of hyperchromatic basaloid cells with nuclear moulding set in a background of a characteristic actinic keratosis (Fig. 1B and C). Immunohistochemically, the basaloid cells expressed cytokeratin-20 (CK20) in a paranuclear dot-like pattern (Fig. 1D) and neuron-specific enolase and lacked expression of S100 protein. A diagnosis of MCCIS in association with actinic keratosis was thus made. The patient underwent subsequent excision by micrographic surgery, which disclosed residual squamous cell carcinoma but not MCCIS.

Table 1 summarizes the clinicopathological features of the present case compared with those from previous reports of MCCIS. This highly uncommon malignancy seems to favor sun-exposed areas, as with conventional MCC, and is associated with more common sun-induced lesions, such as actinic keratosis and squamous cell carcinoma. In the present case, the keratinocytic component of this association defined the clinical picture, but we can speculate that the latter could vary case by case depending on the quantitative representation of each component. Cases associated with a scant MCCIS component are incidental, and are thus due to a fortuitous histopathological discovery.

Serendipity refers to a fortuitous and fortunate finding during the search for something unrelated.9 Therefore, most, if not all of the cases of MCCIS reported to date could be considered serendipitous. There is, however, one major aspect of Horace Walpole’s original definition of serendipity,9 which does not apply here, namely, the ability of linking findings to reach a valuable conclusion. How can we link actinic keratosis and squamous cell carcinoma with MCCIS? We can speculate that this association simply represents a chance collision between two ultraviolet-induced neoplasms. Curiously, the present case is the first example of MCCIS associated with actinic keratosis located on
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Table 1. Clinicopathologic features of the reported cases of Merkel cell carcinoma in situ

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sex, age (years)</th>
<th>Site</th>
<th>Associated lesion</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith et al.²</td>
<td>Male, 84</td>
<td>Arm</td>
<td>Squamous cell carcinoma in situ</td>
<td>Dermal recurrence with regional metastases</td>
</tr>
<tr>
<td>Brown et al.³</td>
<td>Male, 74</td>
<td>Index finger</td>
<td>Squamous cell carcinoma in situ (focal)</td>
<td>No dermal involvement on re-excision</td>
</tr>
<tr>
<td>Al-Ahmadie et al.⁴</td>
<td>Male, 79</td>
<td>Dorsal wrist</td>
<td>Squamous cell carcinoma in situ</td>
<td>Not reported</td>
</tr>
<tr>
<td>Ferringer et al.⁵</td>
<td>Male, 76</td>
<td>Dorsal hand</td>
<td>Squamous cell carcinoma in situ</td>
<td>No residual tumor on re-excision</td>
</tr>
<tr>
<td>Su et al.⁶</td>
<td>Male, 72</td>
<td>Fourth finger</td>
<td>Trichilemmal cyst</td>
<td>No residual tumor on re-excision; sentinel node biopsy negative</td>
</tr>
<tr>
<td>Reese et al.⁷</td>
<td>Male, 73</td>
<td>Posterior neck</td>
<td>None</td>
<td>No metastasis on radical lymph node dissection</td>
</tr>
<tr>
<td>Kitagawa et al.⁸</td>
<td>Male, 62</td>
<td>Scalp</td>
<td>Seborrheic keratosis</td>
<td>Residual squamous cell carcinoma; no residual MCCIS on re-excision</td>
</tr>
<tr>
<td>Present case</td>
<td>Female, 68</td>
<td>Upper lip</td>
<td>Actinic keratosis</td>
<td></td>
</tr>
</tbody>
</table>

MCCIS, Merkel cell carcinoma in situ.

the face, an area where both neoplasms are more frequent.

We know Merkel cells arranged in single units can be highlighted with the anti-cytokeratin antibody featuring a hyperplastic pattern secondary to actinic damage¹⁰, and in the setting of a hyperplastic actinic keratosis.¹¹ Hence, while we recognize that both MCCIS and squamous cell neoplasms may represent a common response to ultraviolet light, we speculate that their simultaneous occurrence could derive either from divergent differentiation of a common pluripotential stem cell or from metaplasia of neoplastic keratinocytes (‘neometaplasia’) with the acquisition of the phenotype of Merkel cells. The well-recognized occurrence of MCC with squamous cell differentiation¹² would be considered as in keeping with this hypothesis.

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References