Mastocytosis, a group of rare disorders that occur in both children and adults, is characterised by abnormal growth and pathological accumulation of mast cells in one or more organs, most commonly the skin (1). Urticaria pigmentosa (UP) is the most common cutaneous variant. In cases of extracutaneous involvement, systemic mastocytosis (SM) can be diagnosed on the basis of the criteria formulated by the WHO. The course of SM in most patients (90%) is indolent, with more aggressive presentation in only a few.

The incidence of cutaneous melanoma is increasing and although this malignancy and mastocytosis originate from 2 different types of cells (melanocytes from the neural crest and mast cells from haematopoetic stem cells, respectively) they share certain similarities, including expression of the transcription factors MITF and STAT3, and dependence of the growth factor receptor KIT and its ligand stem cell factor for their growth and development (2, 3). We have found 5 published case reports that suggest a relationship between these 2 pathologies. In the first, published in 1979, a patient with nodular mastocytosis developed both melanocytoma and mastocytoma (4). In the second, UP and SM preceded a metastatic melanoma (5) and the third involved combined mastocytoma-junctional naevus (6). In the fourth case, malignant melanoma was diagnosed prior to SM (7). And finally, a patient with telangiectasia macularis eruptive perstans (TEMP), a rare form of cutaneous mastocytosis, was found to have a malignant melanoma (8).

Here, we describe our 4 additional cases and discuss possible associations between these 2 diseases.

### Table I. Characteristics of 4 patients with systemic mastocytosis (SM) and malignant melanoma (MM)

<table>
<thead>
<tr>
<th>Pat. no./Sex</th>
<th>Diagnosis</th>
<th>Age at SM diagnosis (years)</th>
<th>Age at which symptoms began (years)</th>
<th>CD2⁺/CD25⁺</th>
<th>Serum tryptase⁴</th>
<th>CM/UP present</th>
<th>MM type, Localisation, Clark level, thickness</th>
<th>Stage</th>
<th>Age at diagnosis of MM</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M</td>
<td>SM-AHNMD-eo/MCL/HCL</td>
<td>63</td>
<td>63</td>
<td>–/+</td>
<td>190</td>
<td>No</td>
<td>Skin, NOS, II, 0.4 mm, not ulcerated</td>
<td>T1a</td>
<td>65</td>
<td>Died from SM</td>
</tr>
<tr>
<td>2/F</td>
<td>ISM</td>
<td>38</td>
<td>9</td>
<td>+/+</td>
<td>62</td>
<td>Yes</td>
<td>Skin</td>
<td>nk</td>
<td>20</td>
<td>Alive</td>
</tr>
<tr>
<td>3/M</td>
<td>ISM</td>
<td>67</td>
<td>38</td>
<td>–/+</td>
<td>36</td>
<td>Yes</td>
<td>Skin nodular, III, 1.4 mm, not ulcerated</td>
<td>T2a</td>
<td>45</td>
<td>Alive</td>
</tr>
<tr>
<td>4/F</td>
<td>ISM</td>
<td>41</td>
<td>14</td>
<td>–/+</td>
<td>70</td>
<td>Yes</td>
<td>Lymph metastasis, no primary MM identified</td>
<td>IV</td>
<td>40</td>
<td>Died from melanoma</td>
</tr>
</tbody>
</table>

⁴All patients showed spindle-shaped morphology and KIT D816V mutations of mast cells.

### RESULTS

Among our 81 Swedish patients diagnosed with mastocytosis between 2007 and 2011, 4 (5%) were also diagnosed with malignant melanoma (Table I). Three of these patients (nos 2–4) suffered from both UP and SM and none of these were treated with PUVA. Of those with UP, 2 had indolent SM and cutaneous melanoma and are still alive, while one was diagnosed with a melanoma metastasis that proved fatal. Patient no. 1 did not have UP, but an aggressive form of SM with an associated clonal haematologic non-mast cell lineage disorder instead and died later of leukaemia (9). In this patient a KIT D816V mutation was detected in the bone marrow mast cells, but not in the melanoma. Both in the case of our patients and those reported previously, the time point at which the first symptoms of mastocytosis and melanoma appeared is usually not known, making it impossible to determine which of these developed first.

### DISCUSSION

Although based on a small number of SM patients, we found that the risk for melanoma among patients with SM appeared higher than in the general population (5% vs...
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The authors declare no conflict of interest.

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The authors declare no conflict of interest.

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Fig. 1. Melanocytes (top) and mast cells (bottom) can interact and promote the cell growth and other cellular functions through the release of cytokines, e.g., interleukin (IL)-6, IL-8, basic fibroblast growth factor (bFGF), nerve growth factor (NGF) and stem cell factor (SCF). Hepatocyte growth factor (HGF) is bound to the extracellular matrix (ECM) from which it can be released by heparin released from degranulated mast cells. Both mast cells and melanocytes express the SCF receptor KIT. Mast cells in systemic mastocytosis patients exhibit a D816V KIT mutation, which leads to a ligand-independent activation of the receptor. Mutations or amplifications of KIT are less frequent in melanoma.

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