Lupus-like skin Eruptions as Indicator of Disease Progression and Poor Outcome in Patients with Haematological Malignancies

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Cutaneous lupus erythematosus (CLE) comprises a heterogenous group of autoimmune skin diseases with a variety of clinical manifestations. Four different subtypes of CLE are currently distinguished, named acute CLE, subacute CLE (SCLE), chronic CLE (including discoid LE, chilblain LE, and LE profundus), and intermittent LE (LE tumidus) (1). Several trigger factors exist for CLE, including ultraviolet light, infections, drugs, and cigarette smoking. Moreover, solid tumours, especially lung and breast cancer, have been reported sporadically in association with CLE (2). In contrast, the occurrence of CLE in patients with haematological malignancies is very rare. We report here a case series of patients with previously unknown acute myeloid leukaemia (AML), myelodysplastic syndrome (MDS) or chronic lymphatic leukaemia (CLL), who presented with clinical and histopathological features of CLE. These lupus-like skin eruptions were associated with disease progression and poor outcome of the underlying haematological disease.

CASE REPORTS

Between January 2015 and December 2020, 5 patients (4 women and 1 man, mean age at first presentation 67 years, range 52–79 years) were transferred to our department with a suspected diagnosis of CLE. All clinical, histopathological, and haematological characteristics of the patients are shown in Table I.

Skin lesions and histopathology resembled SCLE in 2 patients and LE profundus, acute CLE, and LE tumidus in 1 case each (Fig. S1). All patients had at least 1 previous diagnosis of other autoimmune or rheumatic diseases (e.g. polymyalgia rheumatica or Hashimoto’s thyroiditis). Potential trigger factors for CLE were absent, except for cigarette smoking in patient 5 (Table I). None of the patients received medications known to cause drug-induced CLE (e.g. terbinafine, hydrochlorothiazide, or calcium-channel blockers). Moreover, standardized photoprovocation using ultraviolet (UV)A/UVB-radiation was negative in all patients. Serological analysis including antinuclear antibodies (ANA), anti-double-stranded DNA (anti-DNA) antibodies, and screening for extractable nuclear antibodies (ENA) revealed high ANAs (1:1250) in one patient (patient 5). However, none of the patients showed anti-DNA antibodies or CLE-specific ENAs.

It is notable that 3 patients (patients 1–3) had atypical blasts in the lupus-like inflammatory infiltrates, and additionally showed abnormal blood findings (e.g. immature granulocytes, elevated lactate-dehydrogenase, and monocytosis) at first presentation (Fig. S1). In 2 of them (patients 1 and 3), a diagnosis of AML was made, and both died within 2 months shortly after initiation of chemotherapy. In the other patient (patient 2), MDS with excess blasts was diagnosed 9 months after onset of skin lesions, and this patient died due to transition into AML 2 years after first diagnosis of MDS. In the 2 remaining patients (patients 4 and 5), atypical blasts or signs of leukaemia cutis were absent in the lupus-like skin lesions, but both of them had abnormal blood findings (Table I). In these 2 patients, a diagnosis of CLL (patient 4) and MDS (patient 5) was finally made. Similar to the other cases, lupus-like skin lesions were also associated with poor outcome of the underlying haematological disease.

DISCUSSION

It is well known that several rheumatic disorders may occur as paraneoplastic syndromes, for example dermatomyositis, inflammatory myopathies, rheumatoid arthritis, or vasculitides (3). CLE, specially SCLE, has been reported in association with malignancies such as cancer of the breast, colon, lung, or gastrointestinal tract (4, 5). In contrast, CLE or lupus-like eruptions have rarely been reported in patients with haematological disorders (6–8). Misri et al. (6) reported a 48-year-old woman with a lupus-like butterfly rash that histopathologically revealed superficial and perivascular infiltrates with admixed blast cells. AML was diagnosed 1.5 months before, and the patient died shortly after initiation of chemotherapy with cytarabine. Cedeno-Laurent et al. (7) reported a 52-year-old woman with lupus-like skin lesions clinically resembling both ACLE and SCLE. Histopathology showed interstitial and perivascular lymphocytic infiltrates with prominent interstitial mucin, but absence of atypical blasts. A diagnosis of AML was made, and chemotherapy with idarubicin and high-dose cytarabine was initiated, followed by bone-marrow transplantation. Thomas et al. (8) reported a 34-year-old woman with skin lesions resembling lupus erythematosus tumidus (LET). Histopathology showed perivascular and periadnexal lymphocytic infiltrates with lack of mucin but presence of atypical blasts. The patient was diagnosed to have mixed T/B-cell acute lymphoblastic leukaemia and experienced a complete remission after polychemotherapy followed by bone-marrow transplantation. None of the 3 patients had CLE-specific autoantibodies (6–8). These findings are in line with the characteristics of our patients, showing that women are predominantly affected, autoimmune serology is unremarkable in most cases, and occurrence of lupus-like skin lesions is associated with progression and poor outcome of the underlying haematological disease.
### Table I. Clinical and haematological findings of patients with lupus-like skin lesions

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex, Age</th>
<th>Type of lupus-like skin lesions</th>
<th>Location of lesions</th>
<th>Autoimmune diseases</th>
<th>Autoantibody profile</th>
<th>Histopathological findings of lesions</th>
<th>Haematological findings at first presentation</th>
<th>Outcome</th>
<th>Duration until first diagnosis of AML</th>
<th>Other autoimmune diseases</th>
<th>Additional findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F, 79</td>
<td>Cutaneous LE</td>
<td>Face, proximal arms, thighs, gluteal region</td>
<td>Negative</td>
<td>Negative</td>
<td>Superficial and deep perivascular lymphocytic infiltrates, interface dermatitis, strong interstitial mucin deposition, septal panniculitis, mild inflammatory arthritis</td>
<td>LDH: 392, IG: 2.5×10^9/l, monocytes: 39%</td>
<td>Died 2 months after first diagnosis of AML</td>
<td>0 months</td>
<td>Died 2 months after first diagnosis of AML</td>
<td>AML</td>
</tr>
<tr>
<td>2</td>
<td>F, 79</td>
<td>Subacute cutaneous LE</td>
<td>Face, trunk</td>
<td>Negative</td>
<td>Negative</td>
<td>Superficial perivascular lymphocytic infiltrates, interface dermatitis, papillary dermal lymphocytic infiltration, strong interstitial mucin deposition, septal panniculitis</td>
<td>LDH: 348, IG: 2.2×10^9/l, monocytes: 39%, thrombocytes: 129×10^9/l, LDH: 54,</td>
<td>Died 24 months after first diagnosis of AML</td>
<td>9 months</td>
<td>Died 24 months after first diagnosis of AML</td>
<td>AML</td>
</tr>
<tr>
<td>3</td>
<td>F, 88</td>
<td>Acute cutaneous diffuse LE</td>
<td>Arm, upper trunk</td>
<td>Negative</td>
<td>Negative</td>
<td>Perivascular and periadnexal lymphocytic infiltrates, strong interstitial mucin deposition, strong nuclear dust</td>
<td>LDH: 13; 128, IG: 1.9×10^6/l, monocytes: 19%, monocytes: 20%, monocytes: 20%, monocytes: 20%</td>
<td>Alive and disease-free after 8 months of onset of skin lesions</td>
<td>0 months</td>
<td>Alive and disease-free after 8 months of onset of skin lesions</td>
<td>CLL</td>
</tr>
<tr>
<td>4</td>
<td>F, 57</td>
<td>Subacute cutaneous LE</td>
<td>Neck, upper trunk</td>
<td>Negative</td>
<td>Negative</td>
<td>Superficial and deep perivascular lymphocytic infiltrates, DIF: strong interstitial mucin deposition, strong interstitial mucin deposition, strong nuclear dust</td>
<td>LDH: 355, IG: 2.2×10^9/l, monocytes: 20%, monocytes: 20%, monocytes: 20%, monocytes: 20%</td>
<td>Alive and disease-free after 8 months of onset of skin lesions</td>
<td>12 months</td>
<td>Alive and disease-free after 8 months of onset of skin lesions</td>
<td>CLL</td>
</tr>
<tr>
<td>5</td>
<td>M, 52</td>
<td>LE tumidus</td>
<td>Face, trunk</td>
<td>Negative</td>
<td>Negative</td>
<td>Acute lymphocytic inflammatory dermatitis, papillary dermal lymphocytic infiltration, strong interstitial mucin deposition, septal panniculitis</td>
<td>LDH: 13; 128, IG: 1.9×10^6/l, monocytes: 19%, monocytes: 20%, monocytes: 20%, monocytes: 20%</td>
<td>Alive and disease-free after 8 months of onset of skin lesions</td>
<td>0 months</td>
<td>Alive and disease-free after 8 months of onset of skin lesions</td>
<td>CLL</td>
</tr>
</tbody>
</table>

**Note:**
- **Type of lupus-like skin lesions:** Cutaneous LE (LE), subacute cutaneous LE (SCLE), acute cutaneous diffuse LE (ACLE), LE tumidus
- **Location of lesions:** Face, proximal arms, thighs, gluteal region, face, upper trunk, arm, upper trunk, neck, upper trunk
- **Autoimmune diseases:** Polymyalgia rheumatica, ANCA-positive vasculitis, ANCA, Myeloproliferative syndrome with high platelet counts, Myelodysplastic syndrome with high platelet counts
- **Autoantibody profile:** Negative ANA, Negative ANCA, Negative RF, Negative ANCA (ACA+)
- **Histopathological findings of lesions:** Superficial and deep perivascular lymphocytic infiltrates, May-Grünwald-Giemsa-positive dermatitis, papillary dermal lymphocytic infiltration
- **Haematological findings at first presentation:** LDH: 392, IG: 2.5×10^9/l, monocytes: 39%, LDH: 348, IG: 2.2×10^9/l, monocytes: 39%, LDH: 13; 128, IG: 1.9×10^6/l, monocytes: 19%
- **Outcome:** Died 2 months after first diagnosis of AML, Died 24 months after first diagnosis of AML, Alive and disease-free after 8 months of onset of skin lesions
- **Other autoimmune diseases:** AML, CLL
- **Additional findings:** Absent

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**REFERENCES**


