Demographic and clinical characteristics of cutaneous lupus erythematosus at a paediatric dermatology referral centre

B.Z. Dickey,1 K.E. Holland,2,3 B.A. Drolet,2,3 S.S. Galbraith,2,3 V.B. Lyon,4 D.H. Siegel2,3 and Y.E. Chiu2,3

1Medical College of Wisconsin, Milwaukee, WI, U.S.A.
2Department of Dermatology, Division of Paediatric Dermatology, Medical College of Wisconsin, 8701 Watertown Plank Road Milwaukee, WI, 53226, U.S. A.
3Children’s Hospital of Wisconsin, Milwaukee, WI, U.S.A.
4Madison Medical Affiliates, Milwaukee, WI, U.S.A.

Correspondence
Yvonne E. Chiu
E-mail: ychiu@mcw.edu

Accepted for publication
9 April 2013

Funding sources
None.

Conflicts of interest
None declared.

DOI 10.1111/bjd.12383

Summary

Background Paediatric cutaneous lupus erythematosus (CLE) is uncommon and inadequately described in the literature. Similar to adults, children with CLE develop LE-specific and/or LE-nonspecific skin findings. Similarities and differences in demographics and clinical course between paediatric and adult CLE have not been sufficiently described.

Objectives To detail the demographic and clinical features of paediatric CLE and compare these findings with those reported in the adult literature.

Methods A retrospective chart review was performed of 53 children seen in a paediatric dermatology clinic with cutaneous manifestations of LE.

Results Patients presented with all five major subtypes of CLE, with some notable differences from adult CLE and previously published reports of paediatric CLE. Progression from discoid LE to systemic LE (SLE) did not occur in our cohort. Patients with subacute CLE were more likely than adults to have lesions below the waist as well as concomitant SLE. Sex distribution for CLE in our study was equal prior to puberty and female predominant in post-pubertal patients.

Conclusions Children with CLE have variable clinical presentations and progression to SLE that may be different from adult disease. Specifically, children with acute and subacute CLE may be more likely than adults to have systemic disease; therefore, patients with these subtypes should be monitored closely for evidence of SLE. Study limitations included small patient numbers that may limit the ability to generalize these data and relatively short follow-up intervals.

What’s already known about this topic?
- The demographics and clinical course differ between cutaneous lupus erythematosus (CLE) subtypes in adults.
- Patterns in the demographics and disease course of systemic lupus erythematosus (SLE) differ between children and adults.
- The female to male ratio of SLE is equal until puberty and then becomes female predominant.

What does this study add?
- The demographics and clinical course also differ between CLE subtypes in children.
- Patterns in the demographics and disease course of CLE differ between children and adults.
- The female to male ratio of CLE is equal until puberty and then becomes female predominant.
- Children are more prone than adults to develop CLE subtypes that are more strongly associated with systemic disease.
Lupus erythematosus (LE) is an autoimmune disease that presents as a vast spectrum of clinical manifestations involving many organ systems, including the skin. Dermatological findings of LE are termed cutaneous LE (CLE) and may be classified as either LE-specific or LE-nonspecific. LE-specific cutaneous lesions characteristically show interface dermatitis on histology and include the subtypes chronic CLE (CCLE), subacute CLE (SCLE) and acute CLE (ACLE), each with its own subcategories. LE-nonspecific cutaneous findings, such as vasculitis or alopecia, occur frequently in patients with LE but may also be seen outside LE and do not show histological features characteristic for LE.

There are known differences in demographics and disease patterns between childhood-onset and adult-onset systemic lupus erythematosus (SLE). 

Materials and methods
The study was approved by the Children’s Hospital of Wisconsin institutional review board. A retrospective chart review was conducted of patients aged 0–18 years seen at a pediatric dermatology referral centre from January 2000 to June 2012. The Children’s Hospital of Wisconsin pediatric dermatology clinic serves pediatric patients primarily in the Milwaukee, WI metropolitan area, but also draws referrals from throughout the state of Wisconsin and northern Illinois. Patients were identified by the International Classification of Diseases, 9th revision codes 710.0 (SLE), 695.4 (lupus erythematosus) or 373.34 [discoid lupus erythematosus (DLE)]. Only those children with LE-related cutaneous disease (including LE-specific, LE-nonspecific or neonatal LE) seen in the dermatology clinic were included. The CLE subtype was determined based on clinical, laboratory and pathology findings upon review of the record by two of the authors (B.Z.D. and Y.E.C.). Modified Gilliam criteria were used to classify the subtypes (Table 1). Puberty status was assigned by an age cut-off of 12 years based on U.S. national averages. This study was conducted in Milwaukee, WI, U.S.A.

Results
Overall epidemiology and clinical findings: cutaneous lupus erythematosus
Complete demographic, clinical and laboratory findings are summarized in Table 2. Fifty-three children were included in the study. Of these, 15 patients had neonatal LE and will be discussed separately. The remaining 38 patients had pediatric CLE, either LE-specific CLE, either LE-specific skin disease, LE-nonspecific skin disease, or both. Seventeen had CCLE, six had SCLE and 13 had ACLE; three patients were diagnosed with two LE-specific
subtypes and two patients with three or more subtypes. Fifteen children had LE-nonspecific skin disease. Mean follow-up time was 47.8 months (median 38, range 2–138).

Of the 38 paediatric patients with CLE, 45% were black, 34% were white, 13% were Latino and 8% were Asian. Mean age at onset was 11.7 years (median 12.5, range 2–17). Overall, female patients predominated, with a female to male ratio of 2.2:1; however, there was equal sex distribution in children with prepubertal disease onset before age 12 years (female to male ratio, 1:1), and a striking female predominance in post-pubertal disease onset at or after age 12 years (female to male ratio, 4.5:1). These ratios differed substantially by CLE subtype. Male subjects developed CLE earlier than female subjects, with a mean age of 9.8 years for boys vs. 12.5 years for girls.

Laboratory values by CLE subtype are summarized in Table 3. Laboratory parameters were evaluated at various points during the disease course according to the clinical judgement of the providers. Additionally, not all subjects had laboratory testing performed. Overall, 25 patients (66%) met the diagnostic criteria for SLE. Even in the 13 children who did not meet diagnostic criteria for SLE (12 had CCLE, one had SCLE), laboratory abnormalities were common; five out of 12 had haematological abnormalities, one out of seven had abnormal urinalysis findings, and seven out of 12 had an autoantibody present. Skin biopsy with subsequent histological examination was performed in 21 children, as well as in one infant with neonatal LE.

Topical treatments included corticosteroids and calcineurin inhibitors, while systemic agents included corticosteroids, hydroxychloroquine, mycophenolate mofetil, azathioprine, methotrexate and cyclophosphamide.

### Chronic cutaneous lupus erythematosus

Among the 38 patients with CLE, CCLE was the most common subtype (17 patients, 45%). There were 10 patients with DLE localized to the head, four patients with generalized DLE, two patients with lupus panniculitis, and one patient each with lupus tumidus and chilblain LE. This group had the earliest age of disease onset, with a mean of 9.9 years (median 11, range 2–15). These children had nearly equal female to male sex distribution of 1:1:1, and this group was the most evenly distributed by race. When compared with other patients with CLE, this group was the least likely to have a family history of autoimmune disease, with only 24% of

---

**Table 2** Demographic characteristics, family history of autoimmune disease, lesion distribution and treatment modalities according to lupus erythematosus (LE) subtype

<table>
<thead>
<tr>
<th>LE-specific</th>
<th>SCLE (n = 6)</th>
<th>ACLE (n = 13)</th>
<th>LE-nonspecific</th>
<th>Total childhood</th>
<th>Neonatal LE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCLE (n = 17)</td>
<td>12 (92.3)</td>
<td>10 (66.7)</td>
<td>26 (68.4)</td>
<td>9 (60.0)</td>
<td></td>
</tr>
<tr>
<td>SCLE (n = 6)</td>
<td>5 (33.3)</td>
<td>5 (33.3)</td>
<td>12 (31.6)</td>
<td>6 (40.0)</td>
<td></td>
</tr>
<tr>
<td>ACLE (n = 13)</td>
<td>1 (7.7)</td>
<td>2 (15.4)</td>
<td>2 (25.0)</td>
<td>3 (25.0)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>18 (100)</td>
<td>17 (100)</td>
<td>37 (100)</td>
<td>18 (100)</td>
<td></td>
</tr>
</tbody>
</table>

**CCLE, chronic cutaneous lupus erythematosus; SCLE, subacute cutaneous lupus erythematosus; ACLE, acute cutaneous lupus erythematosus.**
patients reporting autoimmune disease in either immediate or distant family members. This group also had the lowest rates of laboratory abnormalities in haematological, urinary and autoantibody tests. Four patients with localized DLE and one patient with lupus panniculitis were the only ones in the study to be treated with topical therapies alone.

Out of 17 total patients with CCLE, five had concomitant SLE (one with localized DLE, two with generalized DLE, one with localized DLE and lupus panniculitis, and one with chilblain LE). Four of these patients had either pre-existing SLE or concurrent development of cutaneous and systemic disease. Notably, the only patient in the study observed to progress from skin-limited to systemic disease was a female patient who had chilblain LE diagnosed at age 12 years and progressed to SLE at age 16 years. No patient with DLE progressed to SLE over a mean follow-up time of 22.9 months (median 23.5, range 2–56).

#### Subacute cutaneous lupus erythematosus

Subacute CLE was the least commonly observed subtype, present in only six patients (16%). The skin lesions were most often described as being annular (four subjects) or papulosquamous (two subjects), but toxic epidermal necrolysis (TEN)-like lesions were described in one patient who also had annular lesions. Five of the six patients (83%) had concomitant SLE; the remaining patient was followed for 50 months without evidence of systemic disease. Distribution of SCLE lesions on the body was more widespread than in other subtypes, as all six patients had lesions located on at least one other body area in addition to the head. The mean age at onset was 11.3 years (median 12, range 2–16). This was the only group in which no patient reported immediate family history of autoimmune disease; however, three patients (50%) had distant family history. All six patients required systemic therapy, and four were prescribed topical treatment in addition.

#### Acute cutaneous lupus erythematosus

Thirteen patients (34%) were seen in the pediatric dermatology clinic for ACLE lesions; all had previously diagnosed SLE. Two had concomitant CCLE, and three had concomitant SCLE. Seven patients also had LE-nonspecific skin disease. Generalized ACLE was the most frequent type (eight patients), followed by localized ACLE (five patients) and TEN-like ACLE (one patient). Interestingly, the one patient with both generalized and TEN-like ACLE was the same patient who also presented with TEN-like SCLE. Generalized lesions were located on the head (75%), trunk (50%), upper extremities (50%) and/or lower extremities (38%). This group had the highest age at onset, with a mean age of 13.6 years. Female to male ratio was 12 : 1, strikingly higher than in other LE-specific subtypes. Systemic therapy was necessary in all 13 patients, while topical treatment was used adjunctively in nine patients.

#### Lupus erythematosus-nonspecific skin disease

Out of the 38 patients presenting with CLE, 15 (40%) were diagnosed with at least one of the LE-nonspecific skin diseases; all 15 had SLE, and eight also had LE-specific skin disease. The majority had only one LE-nonspecific subtype; however, three patients had multiple subtypes. The most common category of LE-nonspecific skin disease was cutaneous vascular disease (nine patients); three had small-vessel vasculitis, three had Degos-like vasculopathy, and the subtypes periangual telangiectasia, livedo reticularis and Raynaud phenomenon were each
diagnosed in one patient. Additional LE-nonspecific subtypes identified were nonscarring alopecia (four), urticaria (three), bullous SLE (two) and erythema multiforme (one).

Neonatal lupus erythematosus

There were 15 patients with neonatal LE, two of whom were sisters. All 15 patients (100%) had lesions on the head, and six patients (40%) presented with lesions localized to the head only. Seven patients (47%) had mothers with known autoimmune disease, while six patients (40%) had asymptomatic mothers later found to have serum autoantibodies. There were two patients whose mothers did not undergo autoimmune disease testing. Anti-Ro/SSA and anti-La/SSB antibodies were present in 93% and 50% of patients, respectively. Three patients had cytopenia, and six patients had hepatitis; no patients had heart block on electrocardiography.

Discussion

Our study summarizes the demographic and clinical characteristics of paediatric CLE seen at a paediatric dermatology referral centre over a 12.5-year period. Differences in disease course between childhood-onset and adult-onset SLE have been reported, but similar data specific to CLE are lacking.5 This study furthers understanding about CLE in children and elucidates differences between adult and paediatric patients. The limitations of our study were the small study population, relatively short follow-up time, retrospective nature and restriction of subjects to those seen in the paediatric dermatology clinic, thus excluding patients with CLE managed by other departments. Even so, this is the largest cohort of paediatric patients with CLE reported to date, and prospective studies are difficult given the rarity of these disorders in children.

In contrast to adult CLE, where a striking female predominance is seen, we found an equal sex ratio in prepubertal patients diagnosed before age 12 years. After puberty, CLE was more likely to occur in female subjects, with a ratio of 4:5 : 1 in those diagnosed at or after age 12 years. These numbers are comparable to those previously reported for paediatric SLE, where the sex ratio is equal until puberty when a striking female predominance is then seen.8 The peak incidence of CLE at 11–13 years is similar to that seen in childhood SLE and was comparable across CLE subtypes.9 Thus, our findings of sex and age distribution for CLE are different from that of adult CLE but similar to childhood-onset SLE.

Chronic CLE was the most common subtype in our study, with the majority of these children having DLE. The age of onset at 9.9 years and sex ratio of 1:1 : 1 seen in our population are similar to other studies.10,11 A major difference observed in our study compared with the paediatric DLE literature is the rate of progression to SLE. Four patients (29%) had SLE at the time of development of DLE, but of the 10 patients with skin-only DLE, none progressed to SLE after a mean follow-up period of 22–9 months. Our rate of previously diagnosed SLE is similar to the 23–5% of paediatric patients with DLE who also met criteria for SLE observed by Sampaio et al.12 Other studies of paediatric patients with DLE, however, have reported various progression rates of 5–9%, 24% and 26%.10–12 In general, these studies suggest that progression rate is higher in paediatric patients than in adult patients with DLE, who progress to SLE at a rate of 5–10%.13 The low progression rate in our study may be attributed to a shorter follow-up time with a mean of only 22.9 months, compared with means of 36 and 49.8 months in the two studies with the highest progression rates.10,12

Subacute CLE was uncommonly observed in our study population with just six cases over the 12.5-year period. Even though SCLE is uncommon below the waist in adults, many of the children in our study had lesions on their lower extremities.3,4 This may suggest different patterns of sun exposure in the paediatric population. Another key point of difference was that the majority of patients with SCLE (83%) in our study had concomitant SLE, in contrast to adult literature reports of 50%.1,14 As children with SCLE may be more likely than adults to develop SLE, providers must be vigilant in monitoring for evidence of systemic disease and its subsequent complications.

Of all adult and paediatric patients with SLE, the most common LE-specific cutaneous finding is the malar erythema of ACLE, reportedly occurring in approximately 80% of patients.15 Reports differ as to the prevalence in paediatrics specifically, with some authors reporting higher rates of children with malar rash than adults and others describing lower percentages of 50–74%.5,9,16 Our study suggests an even lower prevalence, with only 38% of children with SLE having a malar rash; however, not all children with SLE and typical malar erythema would have been referred to dermatology at our institution (and thus did not meet study inclusion criteria). For all ages, a reported 72% of patients with ACLE meet the criteria for SLE.16 All 13 patients with ACLE in our study met the criteria for SLE, suggesting that isolated ACLE without systemic disease is rare in childhood. Again, this highlights the need for a high level of clinical suspicion for SLE when malar erythema is present.

In general, this study corroborates neonatal LE findings from previous studies, with a predominance of head and neck lesions and approximately half of mothers with known autoimmune disease.15,17 Our female to male ratio of 1:5 : 1 is somewhat lower than the 3:5 : 1 reported by Lee.18 As maternal autoantibodies typically clear within 6–9 months of age, infants with neonatal LE are not expected to progress to SLE or CLE in childhood, although predisposition to development of other autoimmune conditions later in life has been reported.19,20 No children in our study developed another autoimmune disease, although mean follow-up time was only 8.6 months (median 3, range 0–56). There was one patient in our study who had anti-Smith and anti-RNP antibodies instead of anti-Ro and anti-La antibodies, which has been reported in very few cases.18,21

Findings of LE-nonspecific skin lesions are generally similar between our study and previous studies regarding the higher
incidence of cutaneous vascular disease in children than in adults. In all patients with SLE, vasculitis has been reported in 10–20%, and in children this is as high as 42%.1-9 Similarly, 36% of paediatric patients with SLE in our study developed cutaneous vascular disease. Nonscarring alopecia, on the other hand, did not occur as frequently in our study as that reported in the adult literature. This was only seen in 16% of our paediatric patients with SLE.1-22 This may suggest that nonscarring alopecia results from a more chronic disease course, as seen in adults with longstanding SLE, or is under-reported by children and parents. The higher prevalence of vascular complications in children again suggests a more severe disease course than in adults.

In this report, we describe in detail the demographics and clinical features of 53 children with CLE in order to characterize further this uncommon disorder. Important differences between childhood and adult CLE were noted, providing useful information for practitioners caring for children with these rare diseases. Childhood-onset CLE may have a stronger association with SLE than adult-onset CLE. Thus, a vigilant approach to monitoring paediatric patients with CLE for development of systemic illness is recommended. Further studies documenting longer-term morbidity and mortality outcomes comparing childhood-onset and adult-onset patients with CLE are warranted.

References