Case Report

Childhood Systemic Lupus Erythematosus; a Rare Multisystem Disorder: Case Report of a 3-Year-Old Girl in Related Oral Involvement as a Primary Sign

Azadeh Horri 1, Masume Danesh 2, Maryam Sadat Hashemipour 3

1 Dept. of Pediatric Dentistry, Oral and Dental Research Center, School of Dentistry, Kerman University of Medical Sciences, Kerman, Iran.
2 Dept. of Pediatrics, Kerman University of Medical Sciences, Kerman, Iran.
3 Dept. of Oral Health, Oral and Dental Research Center, School of Dentistry, Kerman University of Medical Sciences, Kerman, Iran.

KEY WORDS
Systemic Lupus Erythematosus (SLE)

ABSTRACT
Childhood-onset systemic lupus erythematosus (cSLE) is a severe, chronic, multi-organ and systemic autoimmune disorder characterized by inflammatory and autoimmune reaction in several organs. The occurrence of SLE in children is very rare. About 20% of all SLE cases are diagnosed during the first 2 decades of life and the disease is extremely rare before age of 5 years. In this case report, we explore a 3-years-old girl with SLE that symptoms like Primary Herpetic Gingivostomatitis. Early diagnosis lead to proper treatment of the disease and it is important to decrease oral complications in children. Diagnosis could be improved by introduce new cases to provide valuable information for dentists based on diagnostic criteria, therapeutic steps and complication of treatment of SLE in Children. Therefore, it could be concluded that dentists involved in pediatric dentistry should consider and work out on the clinical signs of SLE in children with history of oral herpesvirus infection.

Corresponding Author: Danesh M, Dept. of Pediatrics, Kerman University of Medical Sciences, Kerman, Iran. Email: dr.masumedanesh@gmail.com Tel: +98-3432115780

Cite this article as:

Introduction
Childhood-onset systemic lupus erythematosus (cSLE) is a severe, chronic, multi-organ, systemic autoimmune disorder characterized by inflammatory and autoimmune reaction in several organs [1-2]. Although the cSLE have the same pathophysiology compared to adult type SLE, but the initial clinical presentation of cSLE is observed more sever [3-8]. In Addition, the abnormal appearance common in this age group is frequently responsible for major diagnostic delay [5]. Most report series are minor [4-10], and bias comes since transfer to tertiary pediatric centers. The incidence of cSLE has been reported vary from 0.3 to 0.9 per 100,000 children-years [11-12]. It has been demonstrated that both renal and central nervous system (CNS) organs tend to be more involved in pediatric patients than in adult [13-14].

Only 20% of all patients with SLE are diagnosed during the first two decades of life and the disease is extremely rare in those below 5 years of age [1, 15]. The diagnosis and treatment of patients with cSLE is based on the European evidence-based recommendations for diagnosis and treatment of cSLE [16]. Although several studies have reported the clinical and laboratory characteristics of patients with cSLE [1, 3, 17], based on literature review, there is no presentation of the disease in younger children (below 5 years of age). In this paper, we report a cSLE case of 3-years-old girl, referred to pediatric department of dentistry school, medical university of Kerman, Iran, to provide a valuable information for dentists to improve diagnostic criteria, therapeutic steps in children with oral complication.

Case Report
A 3-years-old girl was referred to pediatric dentistry department with severe oral lesions with white (keratotic) lesion is seen on palate and buccal mucosa in oral cavity and lips along with odynophagia and inability to
She had general gingival involvement. The girl was treated with nystatin suspension, and her malar rash resolved after a 10-day period. The oral aphthous lesions and the malar rash were exacerbated (Figure 1). Due to the worsening of the lesions after 10 days of treatment, further evaluations were needed. In this step, via CBC diff, biopsy of facial lesion (because of the lack of cooperation of the child to done biopsy from oral lesion) and consultation with a rheumatologist, the SLE was diagnosed based on following data.

Blood investigations revealed a hemoglobin concentration of 15.4 g/dL, and white blood cell count of 13.2×10⁶/L and platelet count of 486×10⁹/L. The lymphocyte percentage was 58% compared to 35% neutrophil. Her erythrocyte sedimentation rate (ESR) was 31 mm at the first hour, and C-reactive protein (CRP) was weekly positive. Her serum creatinine level was 0.52 mg/dL, and blood urea nitrogen (BUN) was 14 mg/dL. Sero logic tests to rule out SLE and other collagen vascular diseases showed positive antinuclear antibody (ANA), negative Anti-dsDNA and positive cytoplasmic antineutrophil cytoplasmic antibodies (C-ANCA). The serum level of C3-C4 complement fractions were reported normal (Table 1). Skin biopsy from the malar rash revealed non-specific chronic inflammation (dermatitis) with mononuclear cells without viral inclusion bodies.

Malar rash for face skin lesion was confirmed. The IgG and shaggy BMZ (Basement Membrane Zone) was positive while IgM and C3 were negative. There was epidermal atrophy, mononuclear cell infiltration and orthokeratosis but there was no blister formation. The pathologist differential diagnosis included lupus erythe-
mephiticus and pemphigus vulgaris. After consult with the neurologist and nephrologist, there was no involvement of the CNS and the renal system according to the normal urinalysis. Based on the clinical findings and the laboratory results (6 out of 11 criteria) the diagnosis of cSLE was confirmed according to the American College of rheumatology (ACR) (Table 2) revised criteria for diagnosis of SLE [18]. The positive criteria included 1) Malar rash, 2) Oral ulcers, 3) Discoid rash (scalp lesions), 4) Photosensitivity in malar rash, 5) Antinuclear antibody, 6) Immunologic disorder (positive ANA, c-ANCA and CRP). A rheumatologist was consulted and oral prednisolone (5 mg, twice daily) and oral Hydroxychloroquine (5mg/kg once daily) was started and the oral Hydroxychloroquine (5mg/kg once daily) was started and the patient was followed in an outpatient basis. After 10 days of therapy, the oral aphthous lesion were recovered and the malar rash disappeared (Figure 2). The patient was able to eat and drink and her weight increased after a month. In 6-month follow-up visit, there was no relapse and no lesion were detected. There was no renal and CNS involvement. The patient was recommended to continue the therapeutic regimen till 6 years of age.

**Table 2**: The 1982 revised criteria for classification of systemic lupus erythematosus

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Malar rash</td>
<td>Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds</td>
</tr>
<tr>
<td>2. Discoid rash</td>
<td>Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions</td>
</tr>
<tr>
<td>3. Photosensitivity</td>
<td>Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation</td>
</tr>
<tr>
<td>4. Oral ulcers</td>
<td>Oral or nasopharyngeal ulceration, usually painless, observed by physician</td>
</tr>
<tr>
<td>5. Arthritis</td>
<td>Nonerosive arthritis involving 2 or more peripheral joints, characterized by tenderness, swelling, or effusion</td>
</tr>
<tr>
<td>6. Serositis</td>
<td>a) Pleuritis—convincing history of pleuritic pain or rubbing heard by a physician or evidence of pleural effusion OR b) Pericarditis—documented by ECG or rub or evidence of pericardial effusion</td>
</tr>
<tr>
<td>7. Renal disorder</td>
<td>a) Persistent proteinuria greater than 0.5 grams per day or grater than 3+ if quantitation not performed OR b) Cellular casts—may be red cell, hemoglobin, granular, tubular, or mixed</td>
</tr>
<tr>
<td>8. Neurologic disorder</td>
<td>a) Seizures—in the absence of offending drugs or known metabolic derangements; e.g., uremia, ketoacidosis, or electrolyte imbalance OR b) Psychosis—in the absence of offending drugs or known metabolic derangements, e.g., uremia, ketoacidosis, or electrolyte imbalance</td>
</tr>
<tr>
<td>9. Hematologic disorder</td>
<td>a) Hemolytic anemia—with reticulocytosis OR b) Leukopenia—less than 4,000/mm&lt;sup&gt;3&lt;/sup&gt; total on 2 or more occasions OR c) Lymphopenia—less than 1,500/mm&lt;sup&gt;3&lt;/sup&gt; on 2 or more occasions OR d) Thrombocytopenia—less than 100,000/mm&lt;sup&gt;3&lt;/sup&gt; in the absence of offending drugs</td>
</tr>
<tr>
<td>10. Immunologic disorder</td>
<td>a) Positive LE cell preparation OR b) Anti-DNA: antibody to native DNA in abnormal titer OR c) Anti-Sm: presence of antibody to Sm nuclear antigen OR d) False positive serologic test for syphilis known to be positive for at least 6 months and confirmed by Treponema pallidum immobilization or fluorescent treponemal antibody absorption test</td>
</tr>
<tr>
<td>11. Antinuclear antibody</td>
<td>An abnormal titer of antinuclear antibody by immunofluorescence or an equivalent assay at any point in time and in the absence of drugs known to be associated with “drug-induced lupus” syndrome</td>
</tr>
</tbody>
</table>

**Discussion**

Infantile SLE is an extremely rare and to the best of our knowledge only 13 cases have been reported in the world [19-20] (Table 3). The clinical course of the cSLE is progressive and associated with more severe symptoms and more progressive course with permanent sequelae [1, 3, 14]. Of the 14 patients reported in the literature, 5 died and 6 developed end-stage renal failure and complication of the CNS. It has been previously demonstrated that the prognosis of infantile SLE with high grade glomerulonephritis is poor [19, 21-22]. It is interesting that our patient had a benign course and did not have any evidence of lupus nephritis or involvement of the CNS. Evidence for a genetic predisposition to SLE in humans is based on the concordance rate (23%-57%) saw in indistinguishable twins and on the relative high frequency of familial cases (8%-12%). Candidate genes or loci for SLE liability have been located on the long-arm of chromosome 1 [23]. Our case had a family history of rheumatoid arthritis for her grandfather and uncle. Previously, Zalian et al. [20] demonstrated that infantile SLE has a more progressive course and is associated with more destructive symptoms in comparison with...
adult. They also reported anemia and thrombocytopenia as frequent findings in infantile SLE, whereas leukopenia is rare. Conversely, leukocytosis has been reported to be more common in infantile SLE [3, 20]. In our case, there was no anemia and thrombocytopenia but the patient had leukocytosis which lymphocyte was dominant. These hematological abnormalities, together with positive ANA and decreased C3-C4 complement fractions, should address the diagnosis of SLE in young children with unexplained fever, irritability, and rash. However, since positive ANA and hypocomplementemia may be because of concomitant infections, these findings have low specificity as diagnostic tools, especially, in this age group, where SLE has a very low prevalence [20]. Currently intravenous cyclophosphamide (IVCY) therapy is considered the standard treatment for both children and adults with severe lupus nephritis [16]. However, in our patient, as there was no evidence of lupus nephritis, we did not administer the IVCY. The efficacy of IVCY in treatment of infantile SLE is yet to be identified. There is only two previous report of successful IVCY treatment, in infantile SLE with lupus-nephritis [19, 22].

As recommended by the European evidence-based recommendations for diagnosis and treatment of cSLE, corticosteroids remain the mainstay of the treatment of infantile and cSLE. All the previously reported cases received high dosages of prednisolone with different responses [3, 19-22]. In the current report, we observed significant and abrupt answer of the symptoms to the initial dose of prednisolone. However, in previously reported cases, the response to the corticosteroids were limited and thus adding other agents were required [3, 19-20]. In conclusion, the rare case of infantile SLE can be treated successfully treated with oral prednisolone. Timely diagnosis and treatment is the key step in treatment of cSLE. The diagnosis in this age group should be based on the clinical suspicion.

**Conclusion**

Childhood-onset systemic lupus erythematosus (cSLE) is extremely rare in those below 5 years. In this article we report the diagnosis and treatment of patient with cSLE case of 3-years’ old girl.

**Acknowledgment**

We would like to thank the patient and her family who participated in this study. We also thanks to Dr. Shakibi, Dr. Ataei, Dr. Sharifi Moghadam for their valuable cooperation.

**Conflict of Interest**

The authors have no conflicts of interest relevant to this article.

**References**


