ARTIGO ORIGINAL

CLINICAL FEATURES OF JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS IN IRANIAN CHILDREN

Moradinejad MH,* Zamani GR,** Kiani AR,*** Esfahani T****

Abstract

Objective: Analysis of the clinical and laboratory features of childhood onset systemic lupus erythematosus (JSLE).

Patients and method: Forty five children, aged below 16, were enrolled in this retrospective multicenter study. All patients fulfilled the American College of Rheumatology revised criteria 1982 for the diagnosis of SLE and had shown clinical manifestations of the disease before the age of 16.

Results: The female to male ratio was 8:1. The mean age at onset was 10.5 (ranged between 3 and 16 years). Thirty patients (66%) were correctly diagnosed before referring to our Center.

The clinical manifestation in different organs were as follows: 40 patients (88.8%) had skin involvement, 35 patients (77.7%) experienced musculoskeletal involvement, 29 children (64.4%) suffered from renal disease, hematological abnormalities were detected in 25 patients (55.5%), 12 patients (26%) had cardiovascular disease, 10 patients (17%) presented central nervous system involvement, and 5 patients (11%) experienced SLE-related pulmonary disease. During the follow up period four patients died, two from renal failure, one from CNS complications of JSLE, and one due to severe sepsis.

Conclusion: Clinical manifestations of Juvenile SLE are diverse and often severe. Similar studies should be undertaken in different geographic areas in order to provide a good insight of the disease towards a correct diagnosis of JSLE.

Keywords: Juvenile Systemic Lupus Erythematosus; JSLE; Clinical Features; Iran.

Resumo

Objectivo: Análise das características clínicas e laboratoriais do Lúpus Eritematoso Sistémico de início Juvenil (LESJ).

Doentes e métodos: Quarenta e cinco crianças de idade inferior a 16 anos foram incluídas neste estudo retrospectivo, multicêntrico. Todos os doentes preenchiam os critérios revistos do American College of Rheumatology de 1982 para o diagnóstico de LES e apresentaram as primeiras manifestações clínicas antes da idade de 16 anos.

Resultados: A relação sexo feminino/sexo masculino foi de 8:1. A idade média no início da doença foi de 10,5 anos (entre 3 e 16 anos). Trinta doentes (66%) foram correctamente diagnosticados antes da referenciação ao nosso Centro.

A incidência de manifestações clínicas em diferentes órgãos foi a seguinte: 40 crianças (88.8%) apresentaram envolvimento cutâneo, 35 crianças (77.7%) tiveram envolvimento musculoesquelético, 29 crianças (64.4%) apresentaram doença renal, alterações hematológicas foram detectadas em 25 crianças (55.5%), 12 crianças (26%) tiveram doença cardiovascular, 10 crianças (17%) apresentaram envolvimento do sistema nervoso central e 5 crianças (11%) apresentaram doença pulmonar relacionada com o LES. Durante o período de follow up, quatro crianças morreram, dois por insuficiência renal, um por envolvimento do SNC e um por sépsis grave.

Conclusão: As manifestações clínicas do LES Juvenil são variadas e frequentemente graves. Estudos semelhantes devem ser realizados em diferentes áreas geográficas de forma a providenciar uma boa visão da doença para o correcto diagnóstico do LESJ.

Palavras-chave: Lúpus Eritematoso Sistémico Juvenil; LESJ; Manifestações Clínicas; Irão.
Introduction

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with a wide spectrum of clinical and immunological abnormalities. SLE is primarily a disease of young adult women; however, in 10-15% of patients, the diagnosis is first established during childhood. According to previous reports, Juvenile Systemic Lupus Erythematosus (JSLE) is rarely seen in children under 5 years of age and the peak incidence of childhood SLE occurs around puberty.

The clinical manifestations of the disease, which are remarkably diverse, include fever, erythematous rash, polyarthralgia and arthritis, polyserositis, anemia, thrombocytopenia, renal, neurological and cardiac abnormalities such as pericarditis, myocarditis and endocarditis. The importance of JSLE derives from the fact that it is a life-threatening, long-term illness associated with significant complications. Moreover, the atypical presentation, common in this age group, is often responsible for major diagnostic delay. In patients with childhood-onset SLE, the initial symptoms have been reported to be more severe than in adults. Most studies of JSLE affecting children below the age of 16, have been reported from centers in North America or Europe.

Taking into consideration the different clinical and epidemiological presentations in various ethnic groups, the aim of our study was to review the clinical and laboratory features of 45 Iranian children with SLE.

Patients and Methods

We conducted a retrospective chart review study from May 1996 up to April 2006 in order to describe clinical manifestations and laboratory features among Iranian children with JSLE. The study protocol was approved by the Ethics Committee of the faculty.

The inclusion criteria were as follows:
1. Age ≤16 at diagnosis;
2. Fulfilling the revised American College of Rheumatology (ACR) 1982 criteria for the diagnosis of SLE;
3. Absence of drug induced SLE.

Children with systemic juvenile idiopathic arthritis, polymyositis and vasculitis were excluded from the study.

Results

A sample of 45 patients with JSLE, aged between 3 and 16 years at the diagnosis of disease was studied. Forty patients (88.9%) were female and 5 (11.1%) were male (F to M ratio 8:1). Thirty five patients (77.7%) were from North-West of Iran (Kurdistan, and Azerbajian) and the rest (22%) were from other ethnicities.

The mean age at disease onset was 10.5 ± 2.5 years. The majority of our study group had the diagnosis made within a few months of presentation and only 13% of patients had a delay in diagnosis up to five years. Most of the patients were referred to our centers within a few months of diagnosis, with an average of 3.5 months.

JSLE was correctly diagnosed at onset of the disease in 30 out of 45 patients (66.6%), whereas, the true diagnosis was established with delay in the other patients: leukemia and lymphoma, systemic onset juvenile idiopathic arthritis (SOJIA), immune thrombocytopenic purpura, and rheumatic fever, were among incorrect diagnosis initially made in the early stages of the disease in the rest of our patients.

Constitutional manifestation including fever and weight loss, were present in 43 patients (95%) with JSLE (Table I). The most common feature of the disease at onset was mucocutaneous involvement which affected 40 out of 45 patients (88.8%).
Table I. Clinical presentations of JSLE

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Constitutional</td>
<td>43</td>
<td>95</td>
</tr>
<tr>
<td>Mucocutaneous</td>
<td>40</td>
<td>88.8</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>35</td>
<td>77.7</td>
</tr>
<tr>
<td>Renal</td>
<td>29</td>
<td>64.4</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>12</td>
<td>26.6</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>8</td>
<td>17</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>5</td>
<td>11.1</td>
</tr>
</tbody>
</table>

Table II. Mucocutaneous manifestation

<table>
<thead>
<tr>
<th>Cutaneous manifestation</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Butterfly Rash</td>
<td>30 (75)</td>
</tr>
<tr>
<td>Alopecia</td>
<td>21 (52)</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>15 (37)</td>
</tr>
<tr>
<td>Non specific generalized Rash</td>
<td>10 (25)</td>
</tr>
<tr>
<td>Discoid lesion</td>
<td>9 (25)</td>
</tr>
<tr>
<td>Cutaneous Vasculitis</td>
<td>8 (20)</td>
</tr>
<tr>
<td>Mucosal ulcer</td>
<td>8 (17)</td>
</tr>
</tbody>
</table>

The frequency of various cutaneous manifestations is shown in Table II.

Musculoskeletal involvement was documented in 35 (77.7%) children. Arthritis in our patients was a non-deforming, self limited polyarthritis. Arthritis and arthralgia affected 35 (77.7%) patients. Muscle weakness and myositis was present only in 5 (11.1%) children (Table III).

Twenty nine children (64.4%) experienced renal involvement during the disease course. Hematuria and proteinuria were present in 25 (55.5%) and 22 (48.8%) patients respectively. BUN and Cr increased in 15 (33.3%) of our patients and 26 (57%) underwent renal biopsy. The results are summarized in Table IV.

Cardiovascular problems occurred in 12 patients (26.6%). Pericarditis and myocarditis, affected 7 (58.3%) and 4 (33.3%) children, respectively. Libmann-Sacks endocarditis was quite rare; it was seen in 2 (16.6%) patients during the disease course (Table V).

CNS involvement (documented in 8 patients, 17%) was manifested by non-organic brain disease and psychosis, each in 6 patients (13.3%) and seizure in 5 (11.1%) children; respiratory manifestations were present in 5 (11.1%) patients (Table V).

Anemia was the most common hematological abnormality in our patients (25 out of 45 patients), of which 15 were Coombs’ negative and 10 Coombs’ positive (Table VI). Leucopenia and thrombocytopenia were present in 8 (17%) and 6 (13%) patients respectively. Overall, 16 patients (35%) were Coombs’ positive and 12 patients (26%) were VDRL positive (Table VI). ANA was detected in 43 patients (96%). The results of anti-dsDNA, antiphospholipid antibody, anti-Sm antibody and complement activity are summarized in Table VI.

Conclusion

This is the first report of JSLE from Iran, describing the course of 45 Iranian children with this relatively rare connective tissue disease. According to previous studies, the clinical manifestations of JSLE are similar to those of adults, but with more severe multiorgan involvement. As mentioned, almost 78% of our patients were from North-West of Iran (Kurdistan, and Azerbaijan). This could be due to genetics predisposing factors and HLA associations in this part of Iran. Mucocutaneous involvement was found in almost 89% of our patients at disease onset. Compared to series reported from Europe and the Middle
East, mucocutaneous involvement at onset of JSLE seems to be more frequent in Iranian children what may be due to problems with low education and hygiene.

Arthritis and arthralgia were seen in 78% of our patients. This figure is less than that of Egyptian children (100%). However, in comparison with France, Saudi Arabia, and United States of America our children more frequently experienced joint involvement. According to published reports, the manifestations of muscle involvement can range from generalized muscle ache in 40–80% of patients to frank inflammatory myositis in 5–11% of cases. The histological appearance of muscle in patients with myositis secondary to lupus may be identical to that of patients with polymyositis. Muscle weakness and myositis was noted in five cases (11%), which was almost similar to mentioned report.

Clinically significant renal involvement in systemic lupus erythematosus is more common in children than in adults. At the time of diagnosis of SLE, 75% of children may be found to have renal involvement ranging from minor findings on urinalysis to significantly decreased renal function. Almost 65% of our patients presented renal involvement at onset of the disease, similar to reports from Saudi Arabia and France. Fifty seven percent of our patients underwent renal biopsy. Overall, 15 out of 45 (33.3%) had stage IV WHO renal involvement and 2 out of 45 (4.4%) had stage V WHO renal disease. Lupus can involve all parts of the heart. Twenty six out of 45 children with JSLE presented cardiac involvement at onset of the disease. Our patients were more likely to develop cardiac disease in comparison to French children, however, this figure seems to be lower compared to other reports.

Pulmonary involvement has become increasingly recognized as a manifestation of SLE. Although it usually runs a benign course, pulmonary lupus sometimes carries a serious prognosis. 11.1% of our patients experienced pulmonary disease. This problem is less frequent in our patients compared to Saudi Arabians and French children.

Significant neuropsychiatric (NP) is seen in SLE, most presented as severe non organic manifestations. Neuropsychiatric complications occurred in 50% of JSLE patients. The incidence of CNS involvement in our series is similar to that of reported in France, but significantly less than that of other reports. The lack of systematic neuropsychological evaluation might be the cause of this low frequency of subtle CNS changes. However, compared to another report, we observed higher incidence of psychosis and seizure in our patients.

The majority of our patients suffered from anemia (55%), 40% Coombs’ positive comparable to other series. We observed significantly lower incidence of leucopenia in our children in comparison with other study groups.

The mean titer for ANA was between 1:1280 and 1:640. ANA and anti-ds-DNA antibodies were de-
tected in 96% and 91% of our patients, respectively. This is comparable to what is reported in Saudi Arabia, but our patients were more frequently found to have anti ds-DNA antibody compared to reports from United States. Hypocomplementemia strongly suggests the diagnosis of lupus and identifies patients at increased risk for glomerulonephritis. Our results were similar to those reported from France with regard to low level of complement. We observed significantly lower incidence of anti-Sm antibody in our patients compared to children of other races. The high positivity of ANA and anti ds-DNA, in addition to low complement level, at presentation of the disease suggest that these are helpful tests in diagnosing children suspected to have JSLE.

In conclusion, clinical manifestations of JSLE obviously differ in different races and ethnic groups. It is strongly recommended that similar studies be undertaken in different geographic areas in order to provide a good insight towards correct diagnosis of JSLE.

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