PATTERN AND PROGNOSIS OF HAEMATOLOGICAL AND NON-HAEMATOLOGICAL PRESENTATIONS OF JUVENILE SLE: FIVE YEARS LONGITUDINAL STUDY

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KEY WORDS: JUVENILE SLE, PATTERNS OF PRESENTATION, PROGNOSIS.

ABSTRACT

Objective: To assess the pattern of hematological disorders in juvenile systemic lupus erythematosus (SLE) and its impact on prognosis and survival. The prevalence of SLE in a Pediatric Hematology Unit was also assessed through a five years longitudinal study.

Methods: A prospective follow up study of 32 SLE patients diagnosed and treated in the Children's Hospital and in the Rheumatology & Rehabilitation Department, Ain Shams University Hospitals, during a period of 5 years was done. Follow up of patients with acquired hematological diseases (n=235) diagnosed in a Pediatric Hematology Unit, in the same period was done to assess the prevalence of SLE in that population.

Results: Among the 32 SLE patients, 30 were females and two were males, the mean age at diagnosis was 13.3 ± 3.5 years. Fifteen patients had an initial hematological presentation. Anemia and thrombocytopenia were the
commonest hematological presentation (68.8% and 40.6% respectively). The main non-hematological presenting features included nephropathy (71.9%), cutaneous manifestations (50%) and arthritis (65.6%).

At presentation, ANA antibodies and anti DNA were positive in 67.7% and 67.8% respectively, reaching values of 90.4% and 86.4% respectively during follow up. As regard fate, 25.2% were in remission, 15.6% lost follow up and 59.4% had progressive disease. Ten children out of the studied 235 patients with acquired hematological diseases (4.3%) developed four or more American College of Rheumatology criteria for the diagnosis of SLE during five years follow up. They were 5 out of 186 children with idiopathic thrombocytopenic purpura (2.7%), 2 out of 12 with autoimmune hemolytic anemia (16.7%), 2 out of 3 with Evan’s Syndrome (66.6%) and 1 out of 5 with pure red cell aplasia (20.0%). None of hypoplastic anemia (n=29) developed SLE.

Conclusions: Hematological disorders are common features in childhood SLE with an impact on the prognosis. SLE constitutes the underlying pathology in 4.3% of children with acquired hematological disorders.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a disease of unknown etiology, which at onset may involve only one organ system or be multisystemic. SLE of childhood is a complex and challenging disease, which can occur at any age. Early diagnosis and appropriate management lead to improved outcome for an individual child (Suliaman et al., 2000). SLE results from several related autoimmune processes, although the exact mechanisms of how the disease arises in susceptible individuals remain obscure (Cameron, 1999). The pathology of SLE is characterized by tissue and cellular damage, secondary to production of autoantibodies and deposition of immunocomplexes. (Russo et al., 2000). The manifestations range from mild symptoms to life-threatening events such as thromboses and strokes. Lupus nephritis is one of the most common complications of SLE. Although once considered rare, SLE now appears to be relatively common in certain subsets of the population (McAlindon,
2000). Genetic factors are important in determining both predisposition to nephritis, outcome and response to therapy \((Davis\ et\ al.,\ 1996)\).

SLE has a considerable impact on the health-care system and society. Improvement in control of disease activity and prevention of end-organ damage may reduce costs \((Sutcliffe\ et\ al.,\ 2001)\).

**Aim of Work:**

The aim of the present study was to assess the pattern of hematological disorders in juvenile SLE and its impact on prognosis and survival. The prevalence of SLE as the underlying pathogenesis among children with acquired hematological disorders in a Pediatric Hematology Unit was also assessed.
SUBJECTS AND METHODS

A prospective follow up study of 32 SLE patients diagnosed and treated in the Children's Hospital and in Physical Medicine and Rehabilitation Department, Ain Shams University was done. For inclusion in the study, patients were required to meet four or more of the American Rheumatism Association's (ARA) criteria for diagnosis of SLE (Tan et al., 1982). The following parameters were registered: name, date of birth, gender, date of onset and diagnosis of SLE, clinical manifestations, types of therapy, prognosis, date and cause of death. Clinical manifestations included arthritis, manifestations suggestive of hematological disorders (as anemia, purpura and other bleeding manifestations and thrombosis), neuropsychiatric manifestations (as seizures, psychosis and other CNS lesions), serositis (as pericarditis and pleurisy), mucocutaneous diseases of various types, and renal disorders (including proteinuria, hematuria, oliguria and impaired renal functions).

Disease onset was defined as the time, the first signs or symptoms consistent with lupus, were noted. Date of diagnosis referred to first appearance of four or more of ARA criteria. Duration of follow up was calculated as the interval from disease onset of SLE to the end of the study, lost contact or death. SLE patients were divided into two groups. Group I included children, who initially presented with manifestations of hematological disorders and group II, those presented with non-hematological manifestations.

Patients with acquired hematological disorders (n=235) diagnosed in the Pediatric Hematology Unit, during the same five years period were followed to assess the prevalence of SLE in this population. The children with acquired hematological disorders included 186 patients with idiopathic thrombocytopenic purpura (ITP), 12 patients with autoimmune hemolytic anemia (AIHA), 3 patients with Evan's Syndrome (AIHA and thrombocytopenia), 5 patients with pure red cell aplasia, and 29 patients with hypoplastic anemia.

Laboratory Findings:

The following investigations were done for the included patients: complete blood picture, reticulocytic count, direct and indirect coombs' test, erythrocyte sedimentation rate, liver and renal functions tests, as well as
complete urine analysis and assessment of 24 hours albumin excretion in urine. Detection of anti-nuclear antibodies (ANA) and anti-double stranded DNA antibodies (anti dsDNA) were done by indirect immunofluorescence assay supplied by IMMCO Diagnostic (USA) (Tan et al., 1982). Bone marrow aspiration was done for patients with thrombocytopenia and in suspected bone marrow failure.

**Statistical analysis:**

Data entry and statistical analysis was done using SPSS under windows, version 8. Chi square test of significance was used in order to detect the difference in proportions between groups. Fisher's exact test was used when there was a cell in the 2x2 table with an expected frequency below 5. Kaplan Meier analysis was used to examine the effect of individual clinical and laboratory factors on survival. Difference in survival between groups was tested for statistical survival using log rank test. The independent significance of potentially important prognostic factors on SLE survival was estimated using multivariate Cox regression analysis. P value less 0.05 was considered significant.

**RESULTS**

Out of the 32 patients with SLE, 30 were females (93.8%) and 2 males (6.3%) with male to female ratio 15: 1. The mean age at disease onset was 11.6 ± 2.8 years (range 6-17 years) and the mean age at diagnosis of SLE was 13.3 ± 3.5 years (range 7.5 to 20.3 years). The interval between the time of onset of SLE and its diagnosis was 3.3 ± 2.8 years (range 7 months to 11.2 years). Fifteen patients (46.9%) presented with hematological manifestations (being the only findings in 10 patients) and 17 patients (53.1%) had non-hematological presentations (predominantly renal in 7 patients and mucocutaneous and/or musculo-skeletal in 10 patients).

Table (1) reveals that the most common clinical manifestations among the SLE patients, during 5 years follow up, were nephropathy (71.9%), arthritis (65.6%), purpura &/or ecchymoses (40.6%), malar rash (28.1%) and skin rash (28.1%). Patients in group I had purpura &/or ecchymoses and hemolytic anemia as the main presentation occurring in 60% and 46.7% respectively. Children in group II had a higher incidence of nephropathy (76.5%) and malar rash (41.2%) compared to group I (66.7%
& 13.3% respectively), with no statistically significant difference between the two groups (p>0.05).

Table 1: Clinical manifestations and laboratory investigations during 5 years follow up of SLE patients: divided into two groups according to hematological or non-hematological initial presentations.

<table>
<thead>
<tr>
<th></th>
<th>Total SLE children No. =32</th>
<th>Hematological GROUP I No. =15</th>
<th>Non-hematological GROUP II No. =17</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical manifestations</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at onset in years (X ±SD)</td>
<td>11.6 ± 2.8</td>
<td>11.9 ± 3.4</td>
<td>11.4 ± 2.2</td>
<td>NS</td>
</tr>
<tr>
<td>Age at diagnosis in years (X ±SD)</td>
<td>13.3 ± 3.5</td>
<td>15.1 ± 3.6</td>
<td>11.8 ± 2.5</td>
<td>0.007</td>
</tr>
<tr>
<td>Female sex</td>
<td>30 (93.8)</td>
<td>13 (86.7)</td>
<td>17 (100)</td>
<td>NS</td>
</tr>
<tr>
<td>Malar rash</td>
<td>9 (28.1)</td>
<td>2 (13.3)</td>
<td>7 (41.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>5 (15.6)</td>
<td>3 (20.0)</td>
<td>2 (11.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Maculopapular skin rash</td>
<td>9 (28.1)</td>
<td>4 (26.7)</td>
<td>5 (29.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Arthritis</td>
<td>21 (65.6)</td>
<td>11 (73.3)</td>
<td>10 (58.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Serositis</td>
<td>5 (15.6)</td>
<td>1 (6.7)</td>
<td>4 (23.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>23 (71.9)</td>
<td>10 (66.7)</td>
<td>13 (76.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Neuropathy/or psychosis</td>
<td>7 (21.9)</td>
<td>5 (33.3)</td>
<td>2 (11.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Purpura/or ecchymosis</td>
<td>9 (28.1)</td>
<td>9 (60.0)</td>
<td>0 (0.0)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
<td>7 (21.9)</td>
<td>7 (46.7)</td>
<td>0 (0.0)</td>
<td>0.0019</td>
</tr>
<tr>
<td>PUO**</td>
<td>2 (6.3)</td>
<td>1 (6.7)</td>
<td>1 (5.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Raynaud's phenomenon</td>
<td>5 (15.6)</td>
<td>2 (13.3)</td>
<td>3 (17.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Gangrene of extremities</td>
<td>3 (9.4)</td>
<td>2 (13.3)</td>
<td>1 (5.9)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Laboratory investigations</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANA +ve</td>
<td>29 (90.6)</td>
<td>13 (86.7)</td>
<td>16 (94.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Anti ds-DNA * +ve</td>
<td>19 (86.4)</td>
<td>9 (81.8)</td>
<td>10 (90.9)</td>
<td>NS</td>
</tr>
<tr>
<td>LE test +ve</td>
<td>3 (9.4)</td>
<td>3 (20.0)</td>
<td>0 (0.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Initial hemoglobin &lt; 11gm/dl</td>
<td>22 (68.8)</td>
<td>12 (80.0)</td>
<td>10 (58.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Initial platelets &lt; 100,000/dl</td>
<td>13 (40.6)</td>
<td>11 (73.3)</td>
<td>2 (11.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Initial TLC &lt; 4000/dl</td>
<td>3 (9.4)</td>
<td>1 (6.7)</td>
<td>2 (11.8)</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Anti-double stranded DNA antibodies were tested for only 22 patients, 11 patients in each group
**PUO: pyrexia of undetermined origin  NS: not significant, p value > 0.05

Neuropsychiatric manifestations were found among 21.9% of children, more common among group I compared to group II with no
significant difference between the two groups. The frequencies of other clinical features included serositis (15.6%), photosensitivity (15.6%), Raynaud's phenomenon (15.6%) and peripheral gangrene (9.4%), with no significant differences between the two groups, p > 0.05 (Table 1).

Table 2: Immunological findings at disease onset and during follow up for a sample of the studied SLE patients.

<table>
<thead>
<tr>
<th>Immunological findings</th>
<th>GROUP I Hematological presentation n = 15</th>
<th>GROUP II Non-hematological presentation n = 17</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Isolated No. (%)</td>
<td>With other SLE criteria No. (%)</td>
</tr>
<tr>
<td>ANA</td>
<td>1/7 (14.3)</td>
<td>4/5 (80.0)</td>
</tr>
<tr>
<td>At onset*</td>
<td>8/10(80.0)</td>
<td>5/5 (100.0)</td>
</tr>
<tr>
<td>During follow up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-dsDNA</td>
<td>1/6 (16.7)</td>
<td>4/5 (80.0)</td>
</tr>
<tr>
<td>At onset #</td>
<td>4/6 (66.7)</td>
<td>5/5 (100.0)</td>
</tr>
<tr>
<td>During follow up §</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* ANA level was estimated for 27 patients
# * anti-dsDNA antibodies were tested for only 21 patients
§ * anti-dsDNA antibodies were tested for only 22 patients
* Significant difference between total positive cases in the two studied groups, p < 0.05.

During follow up, 9 patients (28.1%) progressed to renal failure, mainly in group II (35.3%) compared to (20%) in group I. Two patients (13.3%) in group I and three patients (17.6%) in group II developed disseminated peripheral vasculitis, which was severe with peripheral gangrene in one patient. In group I, one patient developed deep venous thrombosis with antiphospholipid antibodies, one patient developed SLE-associated vascular changes in the retina, one patient developed endocarditis with heart valve affection and one patient developed autoimmune thyroiditis.

As regards the immunological laboratory findings, ANA and anti-dsDNA antibodies were assessed at presentation for 27 and 21 patients...
respectively; and during follow up, for 32 and 22 patients respectively. The prevalence of ANA seropositivity at presentation was 41.7% in group I and 86.7% in group II. During follow up, these values increased to 86.7% in group I and 94.1% in group II, with no significant difference between both groups. The prevalence of anti-dsDNA antibodies seropositivity was 81.8% in group I and 90.9% in group II at presentation, rising during follow up to values of 81.8% and 90.9% respectively, with no significant difference between both groups (p > 0.05), (Table 2).

Therapeutic modalities included oral steroids for all patients, 12.5% received pulse methyl prednisolone, 18.8% received cyclophosphamide and 46.9% received immunosuppressive drugs as azathioprine. As regards fate, 15.6% were in remission and off therapy, 9.6% were controlled on therapy, 15.6% lost follow up and 59.4% had progressive disease. Eight patients died during the five years follow up, 2 in group I and 6 in group II. Renal failure was the cause of death in 7 patients and one patient died of disseminated severe vasculitis.

Fig 1. Probability of SLE patients survival as regards hematological (mark X) & nonhematological (mark O) presentations, P > 0.05
Impact of clinical and laboratory parameters on survival:

Kaplan Meier survival analysis revealed a better probability of survival among patients with hematological presentation compared to non-hematological presentation but, the difference was not statistically significant, p value of log-Rank test was > 0.05 (Figure 1). Multivariate Cox regression analysis showed that non-hematological presentation was the only significant predictor variable for the occurrence of renal failure and deaths compared to hematological presentations. The risk of this bad prognosis among children with non-hematological presentations was 5 times higher compared to those with hematological presentations (Table 3).

Table (3): Prognostic factors for occurrence of renal failure and death within 5 years among patients with SLE using Cox regression analysis.

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Hazard adjusted odds ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Renal failure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE with hematological presentation</td>
<td>1®</td>
<td>0.03</td>
</tr>
<tr>
<td>SLE with non-hematological presentation</td>
<td>5.7 (1.3-30.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Death within 5 years</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLE with hematological presentation</td>
<td>1®</td>
<td>0.04</td>
</tr>
<tr>
<td>SLE with non-hematological presentation</td>
<td>5.2 (1.1-26.8)</td>
<td></td>
</tr>
</tbody>
</table>

CI Confidence interval  
® Reference group
Other variables such as presence of arthritis, malar rash, renal disorders, positive ANA or positive anti-dsDNA were not predictors for renal failure or death.

Prevalence of SLE among Children with hematological disorders:

Table (4) demonstrates the results of five years follow up period study of 235 children with different acquired hematological disorders attending the Pediatric Hematology Unit, Children’s Hospital, Ain Shams University. Ten children out of the studied 235 patients with acquired
hematological diseases (4.3%) developed four or more diagnostic criteria for SLE during follow up. They were 5 out of 186 children with immune thrombocytopenic purpura (2.7%), 2 out of 12 with autoimmune hemolytic anemia (16.7%), 2 out of 3 with Evan's Syndrome (66.6%) and 1 out of 5 with pure red cell aplasia (20.0%). None with hypoplastic anemia (n=29) developed SLE. Out of 186 children with acute ITP, 101 children developed chronic ITP, including 5 patients who proved to be SLE (5%).

Table (4): Prevalence of systemic lupus erythematosis among patients with acquired hematological diseases in a Pediatric Hematology Unit at five years follow up.

<table>
<thead>
<tr>
<th>Diagnosis at presentation</th>
<th>Total patients (n =235)</th>
<th>Children who developed SLE (n=10)</th>
<th>Duration in months till diagnosis of SLE X ± SD (range)</th>
<th>+ ve ANA during follow up</th>
<th>+ ve DNA during follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n (%)</td>
</tr>
<tr>
<td>ITP</td>
<td>186</td>
<td>79.1</td>
<td>5/186</td>
<td>2.7</td>
<td>29.4 ± 33.2</td>
</tr>
<tr>
<td>AIHA</td>
<td>12</td>
<td>5.1</td>
<td>2/12</td>
<td>16.7</td>
<td>34.0 ± 26.9</td>
</tr>
<tr>
<td>Evan's Syndrome</td>
<td>3</td>
<td>1.3</td>
<td>2/3</td>
<td>66.6</td>
<td>81 ± 74.3</td>
</tr>
<tr>
<td>Pure red cell aplasia</td>
<td>5</td>
<td>2.1</td>
<td>1/5</td>
<td>20.0</td>
<td>48 months</td>
</tr>
<tr>
<td>Hypoplastic anemia</td>
<td>29</td>
<td>12.4</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

ITP: Idiopathic thrombocytopenic purpura  
AIHA: Auto-immune hemolytic anemia

**DISCUSSION**

Studies of childhood onset SLE suggest that age at onset modifies the expression of the disease, in term of clinical presentation, pattern of organ involvement and serological findings (Barron et al., 1993 and Tucker et al., 1995). Juvenile lupus is reported to account for approximately 20% of all lupus patients (Silverman, 1993). The onset of SLE is reported to be rare before the age of 5 years (Font et al., 1998).
The present study included 32 SLE patients. Their ages ranged between 6-17 years at the time of disease onset. The mean age at onset was 11.6 years and mean age at diagnosis was 13.3 years with male to female ratio 1:15. These results are similar to previous studies (Font et al., 1998, Iqbal et al., 1999 and Lo et al., 1999). The male to female ratio was reported as 1: 6.1 and 1:18 in the adult studies of Uthman et al. (1999) and Vila et al. (1999) respectively. In juvenile lupus, Silverman (1993) reported the male to female ratio to be 1:4.5, with higher male incidence compared to the present study. However, female sex is recognized as a major risk factor for development of SLE (Balsalobre et al., 1999). In murine models of lupus, estrogens were found to be precipitating factors in the emergence of lupus, while androgens were found to be protective (Cameron, 1999).

As regard the duration from onset of symptoms to diagnosis, its mean value was 3.3 ± 2.8 years in the present study. It was reported to be two years in the adult study of Coyle & Wernick (1999); while Silverman (1993) described the median time for diagnosis of pediatric SLE from the onset of symptoms to be 1.2 years. Balsalobre et al. (1999) reported an average of four years between clinical presentation and diagnosis in adult SLE patients presenting with immune thrombocytopenic purpura compared to 24 months in the present study.

The current study revealed that the most common clinical manifestations of SLE among the studied patients were nephropathy (71.9%), arthritis (65.6%), mucocutaneous manifestations (50%) and purpura and ecchymosis (33.3%), similar to previous results (Singh et al., 1997, Font et al., 1998 and Iqbal et al., 1999). Neuropsychological manifestations occurred among 21.9% of the studied patients. Seizures were the most common manifestations followed by psychosis. Similarly, other studies reported that neuropathy occurs in 9% to 20% of patients, mainly as seizures (Uthman et al., 1999 and Vila et al., 1999). In most series, they have been uncommon at presentation (Hussain et al., 1999 and Loh et al., 2000). Seizures may result from lupus cerebritis, stroke or severe renal associated hypertension. Cerebritis is usually accompanied by other clinical or serological manifestations of active disease (Coyle & Wernick, 1999).

Although there are many previous publications of juvenile SLE, the strength of the current study is that, unlike many others, it compares children with hematological presentations (1st group) to those with non-hematological presentations (2nd group). Hematological disorders were
found to be the initial manifestations of SLE among 15/32 patients (46.9%), lower percentage (36.7%) was reported by Martinez-Cordero et al. (1991). The present study revealed no significance difference in the mean age at onset of SLE between the two groups, but the mean age at diagnosis was significantly higher among patients with hematological presentations (15.1 years) as compared to the 2nd group. The frequency of hematological diseases as immune thrombocytopenic purpura (ITP) and autoimmune hemolytic anemia (AIHA) were significantly higher among patients with hematological presentations during the 5 years follow up compared to the 2nd group. There were no significant differences between the two groups in the frequency of mucocutaneous, musculoskeletal manifestations, serositis, nephropathy or neuro-psychological disorders.

Anemia was found among 22/32 patients (68.8%). It has been reported that anemia in SLE may result from several mechanisms and more than one may be operative at any time. Anemia of chronic disease is the most common. It may be also due to autoantibodies to red cells as a part of autoimmunity or due to impaired erythropoietin production by kidneys involved in the SLE (Lam & Quah, 1990). Recent study revealed that anemia of SLE is characterized by inadequate erythropoietin response. Anti-erythropoietin antibodies are frequently present in SLE (Voulgarilis et al., 2000 and Schett et al., 2001). Seven patients had autoimmune hemolytic anemia (AIHA) at presentation. Similar to the present findings, it was reported that AIHA usually occurs at the onset of SLE, with low recurrence rate, and it was found to be independently associated with renal involvement and thrombocytopenia (Kokori et al., 2000).

About 40% of patients had thrombocytopenia. The origin of thrombocytopenia in SLE is complicated resulting from accelerated destruction after binding to anti-platelet antibody, sequestration of platelets in the kidney and lysis and/or phagocytosis of circulating platelets by reaction of both anti-phospholipid antibodies and immunocomplex with circulating platelets (Cameron, 1999).

The frequency of renal disorders at disease onset was found to be 21.4%, which increased to 71.9% during follow up, similar to the results reported in juvenile lupus by Silverman et al. (1993), Iqbal et al., (1999) and Niaudet (2000). The severity of renal disease is variable ranging from asymptomatic proteinuria to rapidly progressive renal failure (Font et al., 1998). Progressive renal disease with renal failure developed in 28.1% of the studied patients compared to 4% in the adult study of Vila et al. (1999).
It has been reported that lupus nephritis in childhood usually presents after the age of 10 years, similar to the present results except for one patient who developed lupus nephritis at the age of nine years. *(Cameron, 1999)*.

At disease onset, 41.7% and 45.5% of SLE patients with predominant hematological presentation had ANA and anti-dsDNA antibodies positivity compared to 86.7% and 90.0% respectively in patients with other presentations, with significant differences between both groups. During follow-up, these percentages increased to 86.7% and 81.8% of patients in hematological presentation group compared to 94.1% and 90.9% in the other group. Font et al., 1998 reported also similar frequencies of ANA and anti-dsDNA antibodies in SLE patients (97% and 85% respectively). *Singh et al. (1997)* found that ANA positivity was seen in all children with SLE. All children with lupus nephritis in the present study had anti-dsDNA autoantibodies positive and 88.9% had ANA positive. *Cameron (1999)* stated that patients with lupus nephritis usually show autoantibodies directed against dsDNA. However, it remains uncertain whether the DNA-antiDNA antibody system has a direct role in the pathogenesis of lupus nephritis.

Kaplan Meier survival analysis indicates a better probability of survival among patients with hematological presentations compared to those with non-hematological presentations, but the difference was not significant. Similar results were reported by *Nosent and Swaak, (1991)*. However, with multivariate Cox regression analysis, patients with non-hematological presentations had significantly five times increased risk for the occurrence of renal failure and deaths compared to those with hematological presentations. This may indicate that, despite of no significant difference in the frequency of renal disorders between the two groups, the type, severity and prognosis of nephropathy were worse in the group with non-hematological presentation. This assumption is supported by the fact that eight out of nine patients with progressive lupus nephritis were from the group with non-hematological presentations. Foster and Kelly *(1999)* stated that renal involvement is less amenable to therapy and patients frequently progress to renal failure once they develop lupus nephritis. *Huong et al. (1999)*, also reported that nephritis is the most serious complication of SLE and the strongest predictor of poor outcome.

As regards prevalence of SLE among children with hematological disorders, 5 out of 101 patients with chronic ITP (4.9%) fulfilled 4 or more ACR criteria for SLE during five years follow up. This value is lower than
that reported by adult studies. Prevalence of SLE in adult chronic ITP studies were 8% (Balsalobre et al., 1999), 10.2% (Adachi et al., 1990), 12.1% (Mestanza-Peralta et al., 1997), 26% (Brunner et al., 1999). All these studies support the statement that patients with ITP are at increased risk of having SLE as the underlying pathogenesis and they should be closely monitored for early detection and management of SLE (Hepburn et al., 1997).

AIHA occurring in the context of SLE is frequently associated with the concomitant presence of thrombocytopenia (Evan's syndrome), (Fong et al., 1992). In the present study, two out of three patients (66.6%) with Evan's syndrome proved to have SLE during follow up, while, only 2 out of 12 patients (16.7%) with AIHA at presentation developed SLE. Choudhry et al. (1996) reported the prevalence of SLE in AIHA to be 5% in a series of 21 AIHA patients aged 2 months to 57 years old.

Among children with pure red cell aplasia, 1 out of 5 patients (20%) developed SLE. None of the hypoplastic anemia patients developed SLE. Chute et al. (1996) reported that aplastic anemia is an unusual and rare manifestation of SLE.

Conclusion:

It can be concluded from this study that the presenting manifestations of SLE in children are diverse. Children with initial predominant hematological presentations have a less aggressive form of the disease with low prevalence of severe lupus nephritis and lower mortality. Presence of lupus nephritis carries the worst prognosis. Patients with Evan's syndrome and chronic ITP are at increased risk of SLE, therefore it is suggested that these patients should be closely monitored for SLE, which may take months to years to fulfill the lupus diagnostic criteria.

REFERENCES


محاولة التكهن بالمخاطر الدموية والغير دموية لمرض الذبآنة الحمراء الصبوي: دراسة موضوعية على مدى خمس سنوات

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الهدف:

تحديد نموذج الاضطرابات الدموية في مرض الذبآنة الحمراء الصبوي وأثره على تقدم المرض وفترة البقاء على قيد الحياة.

أيضاً تم تقييم انتشار مرض الذبآنة الحمراء الصبوي في وحدة أمراض الدم للأطفال من خلال دراسة موضوعية على مدى خمس سنوات.
الطريقة:

أجريت دراسة مستقبلية تتبعية لألفين وثلاثين من مرضى الذنبة الحمراء الصبوي حيث تم تشخيصهم وعلاجهم في مستشفى الأطفال وقسم الروماتيزم والتأهيل بمستشفى جامعة عين شمس على مدى خمس سنوات. أيضا تم متابعة مرضى الأمراض الدموية المكثفة (والبالغ عددهم 235 مريض) تم تشخيصهم في وحدة أمراض الدم للأطفال في نفس الفترة بتقويم انتشار مرض الذنبة الحمراء الصبوي في هؤلاء المرضى.

النتائج:

أسفرت نتائج البحث على أنهين وثلاثين من مرضى الذنبة الحمراء الصبوي عن وجود ثلاثون من الأمراض، واثنان من الذكور كان متوسط العمر عند تشخيص المرضى 13.3 ± 3.5 عاما.

15 مريضا تقدموا بأعراض دموية عند بداية المرض، الأوليميا وقيلة عدد الصفائح الدموية كانتا من أكثر المظاهر الدموية شيوعا (68.8 %), 40.6% على التوالي (بينما كانت الأصابة الكلوية (71.9 % ) والأعراض الجلدية (50 %) والالتهابات المفطر. (65.6% ) من أكثر الظواهر الغير دموية شيوعا. عند تشخيص المرض كانت نتيجة الأجسام المضادة للذئبة (أنا) و (د.ن.ا) برابجية في (67.7 %) على التوالي. وقد واصلت الأرفغة تصل إلى (90.4 %) و (86.4 %) على التوالي أثناء متابعة المرضى. أما بالنسبة لاصبر المرض (25.2 %) من المرضى، حدد لهم كموم للمريض، (15.6 %) فقاوا المتابعة و (59.4 %) حدث لهم تقدم في الحالة المرضية.

شرة أطفال من بين 235 حالة عانوا من أمراض الدم المكثفة مما يمثل (4.3 %) تجمع لديهم 4 أو أكثر من معايير مرض الذنبة الحمراء خلال فترة الخمس سنوات المتابعة. هذه الأطفال مثلا خمسة أشخاص من بين 186 طفل عانوا من الأفراد نتيجة نقص أو خلل بالصفائح الدموية الذاتية العلامة (2.7 %) وانا من بين 12 عانوا من أمراض نتائج خلل بالمناعة (16.7 %) و 2 من 3 عانوا من متلازمة أيفان (66.6 %) و مريض واحد من خمسة أصيب بقصور النمو في خلايا الدم الحمراء (20 %).

الاستنتاج:

الاضطرابات الدموية تمثل معلم شائع في مرض الذنبة الحمراء الصبوي و لها تأثير على درجة تقدم المرض

مرض الذنبة الحمراء يمثل نسبة (4.3 %) من الأمراض التي تصاب الأطفال

بالاضطرابات الدموية المكثفة.