Detection of Antinuclear Antibodies in Childhood Rheumatic Diseases

SAMIA NAZ, ASMA MUSHTAQ, ATTIA BARI, HAFIZ TALHA QAYYUM, AMNAH MAQSOOD, TAHIR MASOOD

ABSTRACT

Objective: To determine the positivity and frequency of ANA in various autoimmune diseases in children.

Patients and Methods: This was a cross-sectional observational study carried out at Medical and Immunology & Serology Departments, The Children’s Hospital and The Institute of Child Health, Lahore over a period of 6 months. More than 200 blood samples were taken from different Medical wards and Medical outdoor departments and serology for ANA Elisa testing was done. Out of them, only ANA positive patients were selected. Information recorded in a pre-designed proforma and data was analyzed by SPSS version 16.

Results: Out of 200 patients 45 (22.5%) were ANA positive. Among 45 ANA positive patients, 25 (55.6%) had the diagnosis of SLE, 9 (20%) had MCTD, 5 (11.1%) had Scleroderma, 4 (8.9%) had dermatomyositis, 2 (4.4%) had Polymyositis. A female predominance was also noted with a female to male ratio of 3:1.2. Age of study population ranged from 3 (minimum) to 16 (maximum) years with mean age of 10.29 ± 3.80 years.

Conclusion: ANA Elisa test can be used as a screening tool in clinically suspected rheumatic diseases in children.

Key words: Antinuclear antibodies, systemic lupus erythematosus, mixed connective tissue disease.

INTRODUCTION

Rheumatic diseases of childhood are complex chronic illnesses that represent clinical manifestations of connective tissue of musculoskeletal system, blood vessels and skin. These are rare in children, and when they occur can be challenging to diagnose and difficult to treat. Rheumatic diseases are worldwide in distribution, although there are notable differences in the frequency of same diseases in different racial groups. It has been difficult to establish the extent of childhood rheumatic diseases in defined populations with any accuracy. Most common rheumatic diseases included Juvenile idiopathic arthritis (JIA), Systemic lupus Erythematosus (SLE), Dermatomyositis, Scleroderma and Juvenile idiopathic arthritis (JIA).

A combination of genetic predisposition and environmental factors contribute to the development of autoimmune diseases. Many autoimmune diseases start at a relatively young age and continue throughout the life. They have a disproportionate affect on public health with an estimated annual cost of over 100 billion dollars in the United States alone. Furthermore, most autoimmune diseases are chronic in nature requiring a life time care. Autoimmune diseases affect 8% of the population, 78% of whom are women.

Anti-nuclear antibody (ANA) – Autoantibodies to nuclear antigens are a diverse group of antibodies that react against nuclear, nucleolar or perinuclear antigens. These antigens represent cellular components such as nucleic acid, histone, chromatin, nuclear and ribonuclear protein. Classically, the ANA hallmarks the serologic diagnosis of SLE and included in the classification criteria for SLE of American College of Rheumatology, but finding an ANA is common to most other autoimmune diseases. There are many reports on the prevalence of serum ANA in normal adults and children. The presence of an autoantibody in a patient does not assure a diagnosis of an autoimmune disease. Rather, a positive serologic test in the company of appropriate sign and symptoms helps to support a diagnosis.

Historically, many different methods were used to test for the presence of autoantibody. Today, testing is principally done with enzyme immunosorbent assays (EIA), because of cost saving measures with mechanization. Typically, screening patient’s serum for the detection of an ANA with ELISA, provides high degree of sensitivity.
PATIENTS AND METHODS

This study was conducted in Paediatric Medicine and Immunology & Serology Departments, The Children’s Hospital & Institute of Child Health, Lahore, from September 2011 to February 2012. All patients ranging from 1 year to 16 years who were clinically suspected as rheumatic disease were enrolled in the study. By aseptic technique, 3ml of venous blood was drawn from the patients by trained staff, labeled them with appropriate numbers and sent to the Department of Immunology and Serology for ANA Elisa testing. The ORGENTEC ANA Detect assay is intended for a qualitative enzyme immunoassay (EIA) to screen for the presence of antinuclear antibodies (ANAs) in serum. ANA detect Elisa was negative when < 1.0, borderline between 1.0-1.2, positive when > 1.2. Demographic data and clinical presentation of these patients were noted. All the data was recorded in predesigned proforma and results were analyzed by SPSS version 16. Mean±SD was given for quantitative variables. Frequencies and percentages were given for qualitative variables.

RESULTS

A total of 200 patients were enrolled. Out of them 45 (22.5%) were ANA positive and enrolled in the study for further analysis. ANA Elisa titres range from 1.22-6.20 with mean of 2.87 +/- 0.886. There were 33 (73.3%) females and 12 (26.7%) male with F:M ratio 3:1. Mean age at the time of testing was 10.29 +/- 3.8 years with minimum age of 3 years and maximum of 16 years. Six patients (13.3%) were between 1-5 years of age, 19 (42.2%) were between 6-10 years and 20(44.5%) were between 11-16 years of age. SLE was the most common autoimmune disease associated with ANA positivity (n=25, 55.6%) followed by Mixed connective disease, Scleroderma, dermatomyositis and polymyositis. (Table 1)

Most common clinical presentation was rash (discoid lupus,malar rash, heliotrope rash, vasculitic rash) in 42(93.3%) followed by photosensitivity (88.9%), jaundice (68.9%), renal involvement (66.7%) and arthritis (60%), Raynaud’s phenomenon (42.2%), oral and nasal ulcers (33.3%), muscle weakness (17.8%) and sclerodermal changes (24.4%).(Table 2)

Table 1: Frequency of Rheumatic diseases among ANA positive study group (n=45)

<table>
<thead>
<tr>
<th>Autoimmune Diseases</th>
<th>n</th>
<th>percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic Lupus Erythematosus</td>
<td>25</td>
<td>55.6</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>05</td>
<td>11.1</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td>04</td>
<td>8.9</td>
</tr>
<tr>
<td>Mixed Connective Tissue Disease</td>
<td>09</td>
<td>20</td>
</tr>
<tr>
<td>psitis</td>
<td>02</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Table 2. Clinical findings of Antinuclear antibodies positive patients (n=45)

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>n</th>
<th>percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>42</td>
<td>93.3</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>40</td>
<td>88.9</td>
</tr>
<tr>
<td>Arthritis</td>
<td>27</td>
<td>60.0</td>
</tr>
<tr>
<td>Oral and/or Nasal ulcers</td>
<td>15</td>
<td>33.3</td>
</tr>
<tr>
<td>Jaundice</td>
<td>31</td>
<td>68.9</td>
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<tr>
<td>Renal involvement</td>
<td>30</td>
<td>66.7</td>
</tr>
<tr>
<td>d’s phenomenon</td>
<td>19</td>
<td>42.2</td>
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<tr>
<td>I muscle weakness</td>
<td>08</td>
<td>17.8</td>
</tr>
<tr>
<td>normal changes</td>
<td>11</td>
<td>24.4</td>
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</tbody>
</table>

* Malar rash, Discoid lupus, skin rash, heliotrope rash, vasculitis

DISCUSSION

Antinuclear antibody (ANA) tests are frequently used to screen children for childhood rheumatic diseases. However, the diagnostic utility of this test is limited because of the large number of healthy children who have low-titer positive tests. In our study ANA test was done in 200 patients, who have clinical suspicion of some autoimmune rheumatic disorder, but it was positive in 45(22.5%) patients. Indeed, Malleson and colleagues have shown that ANA test may be positive in as many as 33% of healthy children. Other studies have verified the lack of specificity of ANA test in children.

The most common autoimmune rheumatic disease was SLE in our study, which was found in 25(55.6%) patients. Due to variable clinical presentations with which childhood SLE presents, it is frequently in the differential diagnosis of children presenting with challenging or difficult illnesses. Antinuclear antibodies were positive in 95-99% of individuals with SLE. Though a positive ANA is not required for diagnosis of SLE yet a negative ANA is extremely rare in SLE.

Majority of our patient were female and older than eight years of age. Lehman et al described the same findings in his studies. As majority of patients in our study were of SLE which has the most common clinical presentation of rash, photosensitivity, arthritis and oral ulcers. This is consistent with many other studies.

Children with autoimmune rheumatic diseases are often clinically indistinguishable from other children with positive ANA test in the spectrum of complaints with which they present for initial medical care. However, judicious use of the history, physical examination and thoughtful interpretation of ANA titers will significantly assist in distinguishing children with these illnesses from children with more benign conditions.
CONCLUSION

ANA Elisa titers assist in discriminating children with autoimmune rheumatic diseases from children with other conditions. Patient age, gender and ANA titer are the best measures distinguishing children with autoimmune diseases from ANA-positive children with other illnesses or self-limited conditions. Because of its limited diagnostic specificity and high prevalence of false positive, ANA test should be used to address only when clinical examination is suggestive of some autoimmune rheumatic disease.

REFERENCES