A REVIEW OF GASTROINTESTINAL DISORDERS IN PATIENTS WITH PRIMARY ANTIBODY IMMUNODEFICIENCIES DURING A 10 YEAR PERIOD (1990-2000), IN CHILDREN HOSPITAL MEDICAL CENTER

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ABSTRACT

One of the most prevalent manifestations of primary antibody deficiencies is gastrointestinal disorders.

In this study we reviewed 83 patients including 25 with X-Linked agamaglobulinemia, 40 with common variable immunodeficiency, 14 with IgA deficiency and 4 with IgG subclass deficiency. The mean age of patients was 10 year (1-28yr). The ratio of male to female was 1.5.

Gastrointestinal system was affected in more than half (57.8%) of them. The most common symptom was diarrhea (56.6%) and the most prevalent pathogen was, G. Lamblia.

Other disorders were chronic active hepatitis in 6 patients, ulcerative colitis in 2, small intestinal villus atrophy in 5, nodular lymphoid hyperplasia of small intestine in 3 and chronic gastritis in 4 patients. One patient suffered from abdominal lymphoma.

We found a direct correlation between failure of patients to thrive and the duration of the delay in diagnosing the underlying disease. This difference was more apparent in those with both antibody deficiency and gastrointestinal involvement.

Keywords: Antibody immunodeficiency, gastrointestinal system disorders, failure to thrive.

INTRODUCTION

Primary humoral deficiencies are various immunodeficiencies characterized by restrictive antibody formation either from impaired B-lymphocyte development or failure of effective B-lymphocyte responses to T-lymphocyte signals.

The mucosal immune system has an important role in the homeostasis of the gastrointestinal system, there-

Abbreviations:
GI = Gastrointestinal
XLA = X-Linked agamaglobulinemia
CVID = Common Variable Immunodeficiency
IgA-D = IgA deficiency
IgG-SCD = IgG subclass deficiency
IVIG = Intravenous immunoglobulin
HCV = Hepatitis C virus

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fore the prevalence of serious GI abnormalities in the context of congenital or acquired immunodeficiencies is high.13

Thus such disorders affect markedly the natural course and the final prognosis of those patients.4,5,3,7,8

Without proper nutrients absorption (e.g. due to GI disorders), the immune system would be deprived of the components and mechanisms that are needed to generate an effective immune response.19

Marked growth impairment is found among those suffered from these disorders too.

In this study the diverse GI disorders were reviewed among patients with primary antibody deficiency from the Iranian Primary immunodeficiency association registry.2

We studied different adverse consequences of GI tube involvement such as worsening the natural course of the underlying disorder, failure of growth and other morbidities, in order to determine the mutual effects of immunity and GI system disorders in our patients.

MATERIAL AND METHODS

In this study we selected all patients who were followed up as primary antibody deficient during a 10-yr period (1990-2000) in children hospital, medical center. Their medical diagnosis was revised according to the WHO standard criteria for immunodeficiency disorders.10

A standard questioner was filled up for each patient.

Immunoglobulins were measured by SRID method. IgG sub classes were detected by ELISA. Lymphocyte numbers were counted by flowcytometric analysis.10

Liver function tests were routinely checked every 6 months for those receiving regular IVIG. RT-PCR for HCV detection was used for 15 of them.10

Those with GI disorders had consultation with pediatric gastrointestinal sub specialists, and received advanced services such as endoscopies, biopsies, ...

RESULTS

Table I: Frequency of different antibody deficiency disorders.

<table>
<thead>
<tr>
<th>Disease</th>
<th>No</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>XLA</td>
<td>25</td>
<td>30.1</td>
</tr>
<tr>
<td>CVID</td>
<td>40</td>
<td>48.2</td>
</tr>
<tr>
<td>IgA-D</td>
<td>14</td>
<td>16.9</td>
</tr>
<tr>
<td>IgG-SCD</td>
<td>4</td>
<td>4.8</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>100</td>
</tr>
</tbody>
</table>

Table II. Frequency of GI involvement in patients with primary antibody deficiencies.

<table>
<thead>
<tr>
<th>Disease</th>
<th>with GI Disorders</th>
<th>without GI Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>XLA</td>
<td>15</td>
<td>60</td>
</tr>
<tr>
<td>CVID</td>
<td>25</td>
<td>62.5</td>
</tr>
<tr>
<td>IgA-D</td>
<td>6</td>
<td>42.9</td>
</tr>
<tr>
<td>IgG-SCD</td>
<td>2</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td>57.8</td>
</tr>
</tbody>
</table>

In this study we reviewed 83 patients with antibody deficiency including 25 with XLA, 40 with CVID, 14 with IgA-D and 4 with IgG-SCD. (Table I)

They were 33 girls and 50 boys. Their mean age was 10 yr with the range of 1 to 28 yr.

In forty eight of them (57.8%) GI tract was involved. (table 2)

The most common manifestation was chronic diarrhea (56.6%) (Table III) and the most prevalent enteric pathogen was G. lambia (27.7%). (Figure 1)

Pathological findings showed intestinal villus atrophy in 5 patients, nodular lymphoid hyperplasia in 3 patients and chronic gastritis in 4 patients. Liver biopsies revealed chronic active hepatitis in 5 patients. (Figure 2)

RT-PCR for HCV in 15 patients who had received regular monthly IVIG revealed no positive result.

One of CVID patients suffered from abdominal lymphoma.

There was a report of intestinal malakoplakia in a patient with XLA.

Forty three of our patients with GI complications (68%) had failure to thrive while of those without GI disorders only 28% showed delay of growth.

Of those 43 patients with growth delay one fifth showed mild malnutrition, 3/5 moderate and 1/5 severe malnutrition. (Figure 3) There was a strong correlation between failure to thrive and the length of delay in establishing the proper diagnosis. The mean length of this delay was about 40 months.

DISCUSSION

The antibody deficiencies constitute about 50% of all cases of primary immunodeficiencies. The intestinal mucosal immune system as a first line of defense prevents the entrance of harmful pathogens and macromolecules into inner body environment.

Gut associated lymphoid system consists of many nonimmunologic factors and various immunologic components such as immunoglobulins, especially secretary Ig A, abundant numbers of lymphocytes, etc. If an
Fig. 1. The Results of Stool exams and stool cultures in patients.

Fig. 2. The frequency of Hepatomegaly in Patients.

Fig. 3. The Frequency of failure to thrive.
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Table III. Frequency of diarrhea in patients with primary antibody deficiencies.

<table>
<thead>
<tr>
<th>Disease</th>
<th>with GI Disorders</th>
<th>without GI Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>XLA</td>
<td>14</td>
<td>56</td>
</tr>
<tr>
<td>CVID</td>
<td>25</td>
<td>62.5</td>
</tr>
<tr>
<td>IgA-D</td>
<td>6</td>
<td>42.4</td>
</tr>
<tr>
<td>IgG-SCD</td>
<td>2</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>56.6</td>
</tr>
</tbody>
</table>

antigen escapes this system it would be removed by second line of defense in liver sinusoids before entering the systemic circulation.

Dysfunction of the immune system is frequently accompanied by GI disorders such as recurrent or chronic infections, malabsorption and various autoimmune and malignant transformations.5,6,7,8

In this study we reviewed clinical courses of 83 patients with primary hypogammaglobulinemia from Iran PID registry. Twenty five of them Suffered from XLA, 40 from CVID, 14 from IgA-D and 4 from IgG-SCD. The mean age of our patients was 10 years.

The mean age of GI initial presentation in our study is lower than other studies. It is probably because our patients had been enrolled in a pediatric referral center for ID disorders.9,10

More than half of them suffered from GI tract disorders. Those with CVID showed the most frequent GI tube involvement (62.5%).

The most common symptom was diarrhea and the most prevalent pathogen was G. Lamblia that is about 3 times as much prevalent as in general population.11

Regular follow up of hepatic function revealed 9 cases with elevated liver enzymes. RT-PCR for HCV detection results were negative in these patients while in the study of Bjoro et al there were 21 positive cases from 83 patients receiving regular IVIG. Their population was older than ours thus they had been given IVIG for a longer duration.11

GI histopathologic studies showed chronic gastritis in 4 patients (4.8%), villus atrophy in 5 (5.2%) and nodular lymphoid hyperplasia of small intestine in 3 cases (2.9%). The study of Zullo et al revealed a 41% frequency of chronic gastritis in primary immunodeficiency. The mean age of their patients was about 49 years.11

Autoimmune involvements of GI such as ulcerative colitis were seen in 2 patients with CVID.

There are frequent reports of malignant changes in GI tube of immunodeficients.11,15

One of our patients with CVID had abdominal lymphoma.

The review of growth indices of our patients showed some degrees of growth failure (mild to severe) in 48.2% of them. There was a logical correlation between the severity of the growth impairment and the duration of latency in making appropriate medical diagnosis.

One notably important conclusion of our study is that this failure to thrive is more frequent in those with both GI disorders and antibody deficiency(68%), while it is about 28% in those without GI involvement.

GI tract diseases are among the most prevalent presentations during the natural course of antibody deficiencies. They affect not only the growth indices of patients but also the prognosis and natural course of the immune defect.

We conclude that the sooner the proper disease and GI malaise be diagnosed and controlled the better would be the final outcome of those with humoral immunodeficiencies.

REFERENCES

L. Atarod, et al.