Type 1 Diabetes Mellitus, Celiac Disease, and Selective IgA Deficiency: a Case Report

Mitra Rooin Peikar 1, Sepehr Rasekhi 2, Hosein Hamadiyan 2,*

1 Pediatrics, Clinical Research Development Center of Children Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran
2 Student Research Committee, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

*Corresponding author: Hosein Hamadiyan, Medical Student of Hormozgan University of Medical Sciences, Bandar Abbas, Iran; Email: s.hamadian@yahoo.com; Tel: +989350731548.

Abstract

Patients with Type 1 diabetes mellitus have a high prevalence of celiac disease, symptoms of which are often mild, atypical, or absent. Untreated coeliac disease is associated with an increased risk of malignancy, particularly of lymphoma. Therefore, we report a 9-year-old girl with Coeliac disease, diabetes type 1 and Selective IgA deficiency. A 9-year-old female patient presented in august 2014 with the complaints of constipation, abdominal pain, nausea, vomiting and lethargy. Type 1 Diabetes Mellitus, Coeliac Disease, and Selective IgA Deficiency were diagnosed simultaneously. Response to treatment was good and the patient was discharged a few days later.

Keywords: Type 1 Diabetes Mellitus, Coeliac Disease, Selective IgA Deficiency

Introduction

Coeliac disease (CD) is an autoimmune enteropathy characterized by constipation, short stature, vomiting, diarrhea, weight loss, abdominal distension, and other symptoms caused by vitamin and nutrient deficiencies such as osteoporosis, thyroid problems and iron deficiency anemia (1). It is caused by permanent intolerance to gluten in genetically susceptible individuals. The human leukocyte antigen system (HLA) is the main genetic predisposing factor in disease development, with the strongest effects attributed to two different genes of the class II MHC region: HLA-DQA1 and HLA-DQB1 (2). Multiple genetic studies over the last decade have identified additional genetic variants associated to disease susceptibility (3). Due to these genetic variations, Coeliac disease has been associated with many other HLA-linked disorders such as Selective IgA deficiency (IgAD) and type 1 diabetes mellitus (4). Serologic assays usually exhibit high serum levels of autoantibodies, including endomysial, tissue transglutaminase (tTG), and deamidated gliadin antibodies (IgA and IgG isotypes). Since the IgA isotype usually predominates in coeliac disease, elevated levels of IgA antibodies served as the best serological diagnosis for coeliac disease (5). However, if an individual has an IgA deficiency, then an assay to screen the IgG class of autoantibodies should be ordered (6). In this study, we report a 9-year-old boy with Coeliac disease, diabetes type 1 and Selective IgA deficiency. Written informed consent was obtained from the patient.

Case Report

A 9-year-old female patient presented in august 2014 with the complaints of constipation, abdominal pain, nausea, vomiting and lethargy. Itching and rash were observed generally, since a month ago. Thereafter, pharyngitis was appeared with has treated by antibiotics. However, treatment was not successful completely and she had experienced repeated vomiting, abdominal pain and weakness. In addition, patient's history was contained constipation. Abdominal X ray was ordered for this person and it's findings showed fecal impaction. Bisacodyl suppository was used to treat this problem.

Weakness, anxiety, abdominal pain, polyuria, polydipsia, and palm paresthesia were found a day before admission. Her vaccination was completed and she had no history of previous Hospitalization.
No familial relationship and history of diabetes were observed among parents and family, respectively.

General appearance of patient provided some evidences of failure to thrive (FTT) and atrophic muscles: weight 15kg and height 127 cm. Her physical examination was as follow: BP: 80/60, RR: 35, PR: 95, T:36.6 (Axillary). Kosmall respiration was also found by additional examinations. Tenderness was also observed in preumbilical abdomen. Other Results of her physical examination on admission were normal and unremarkable.

Patient was hospitalized by impression of diabetic keto-acidosis (DKA) with NPO and thereafter she was referred to ICU. Following orders were represented for one hour after admission:

1. Control of vital signs (each 8 hours)
2. Check of BS, CBC' DiFF, BUN, Cr, Na, K, Ca, P, ESR, CRP, ALT, AST, Alkaline Phosphatase, Bilirubin (total and direct), TSH, T4
3. Blood culture
4. Urine analysis and urine culture
5. Heart monitoring
6. Fixing of fully catheter
7. Nasal Oxygen (1-2L/min)
8. Check of VBG (venous blood gas)
9. Ceftriaxone (750mg IV Q 12hr)
10. Normal saline serum (300cc free)
11. ECG

Findings of mentioned tests were documented in table 1. In second hour, 50 unit of regular insulin was mixed with 500cc of normal saline and then 50cc was removed. Of remained solution, 15 drops per min were infused in addition to half saline (81cc+1.6 kcl per hour). Patient was exited from DKA according to table 2.

Based on FTT and diabetes, the case was suspected to coeliac and some examinations were ordered to confirm this diagnosis, as follows:

1. IgA: <0.6 (0.28-2.22) IU/ml
2. Tissue transglutaminase antibody (IgG): >100 <12 IU/ml
3. Tissue transglutaminase antibody (IgA): <0.2 <8 IU/ml

Biopsy endoscopy was conducted to confirm coeliac diagnosis. Duodenojejunal junction biopsy and jejunal biopsy were obtained. Reports of this tests showed normal stomach and esophagus and confirmed the primary decision. Echocardiography was normal. Nutritional counseling was ordered to set a diabetic, high calorie and potassium diet without wheat and barley. Twelve units of Lantus insulin (before sleep) with 4 units neorapid insulin (before each meal) were ordered. Then, the patient was discharged a few days later. Other findings of tests were documented in table 3

**Discussion**

There is an increased prevalence of coeliac disease in patients with Type 1 DM, with rates of up to 10%, depending on the population surveyed and the screening test used (7). The coincidence of the two conditions is in part accounted for by similar genetic backgrounds, each having a high prevalence of HLA B8, DR3, and DQW2 (8). The clinical features of coeliac disease in diabetic patients are generally similar to those in non-diabetic patients. Many have diarrhoea and malabsorption, particularly of iron and folic acid. Symptoms, however, are often atypical and may be absent (9). Features of coeliac disease specific to Type 1 DM include poor glycaemic control and troublesome recurrent hypoglycaemia. Coeliac disease is associated with an increased incidence of malignancy, including squamous cell carcinoma of the oesophagus and adenocarcinoma of the small intestine (10). The highest relative risk is for EATCL, although Hodgkin’s disease also occurs with increased frequency. B cell non-Hodgkin’s lymphoma, as occurred in one of our patients, has not previously been reported in association with coeliac disease (11). Among the features that suggest lymphoma in a patient with coeliac disease are unexplained weight loss, relapse of diarrhoea, pigmentation, abdominal pain, pyrexia, and hepatomegaly (12). Malignancy, and in particular
lymphoma, may be the first manifestation of coeliac disease. There are suggestions of an increased frequency of non-Hodgkin’s lymphoma in patients with Type 2 DM (13). There is no evidence, however, that lymphoma occurs with increased frequency in patients with Type 1 DM. To our knowledge, lymphoma has not been previously reported in patients with Type 1 DM and coeliac disease. Each of these patients had a small bowel histological appearance in keeping with coeliac disease but, because of the severity of their illness, it was not possible in each case to demonstrate improvement on a gluten-free diet (14). Although it has been argued that villous atrophy in patients with EATCL may be a result of the effects of the lymphoma rather than to concomitant coeliac disease, most authorities now agree that many if not all patients with EATCL and villous atrophy have coeliac disease (15). Long-term adherence to a gluten-free diet significantly reduces the relative risk of malignancy. The most sensitive and specific screening test available is IgA endomysial antibody (16). False negative tests can occur in patients with IgA deficiency. Whether formal screening of all patients with Type 1 DM should be undertaken is uncertain. However, a high index of suspicion for coeliac disease is required for all Type 1 diabetic patients with unexplained constitutional or gastrointestinal symptoms (17).

**Conflicts of interest**

Authors declare no conflict of interests.

<table>
<thead>
<tr>
<th>Table 1. Primary Test Report</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Results</strong></td>
</tr>
<tr>
<td>7.21</td>
</tr>
<tr>
<td>12.2</td>
</tr>
<tr>
<td>50.2</td>
</tr>
<tr>
<td>4.9</td>
</tr>
<tr>
<td>-20.6</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>---</td>
</tr>
</tbody>
</table>

*venous blood gas **Base Excess*
Table 3. testing during admission and discharge

<table>
<thead>
<tr>
<th>Results</th>
<th>Testing during hospitalization</th>
<th>Tests discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yellow Clear 5 1005</td>
<td>Urine analysis Color Appearance PH Specific Gravity</td>
<td>Total bilirubin 0.7mg/dl</td>
</tr>
<tr>
<td>Trace</td>
<td>Protein 0.3 Direct bilirubin 2.5 TSH</td>
<td>131</td>
</tr>
<tr>
<td>Glucose 2+</td>
<td>Blood 9</td>
<td>4.6</td>
</tr>
<tr>
<td>Hemoglobin negative</td>
<td>Trace</td>
<td>T4</td>
</tr>
<tr>
<td>Bilirubin negative</td>
<td>Urine analysis</td>
<td>Albumin</td>
</tr>
<tr>
<td>1+</td>
<td>Granular cast</td>
<td>SGPT 16</td>
</tr>
<tr>
<td>WBC 1-2</td>
<td>SGOT</td>
<td>7.48</td>
</tr>
<tr>
<td>RBC 1-2</td>
<td>PO2</td>
<td>PH</td>
</tr>
<tr>
<td>EP 2-3</td>
<td>PCO2</td>
<td></td>
</tr>
</tbody>
</table>

References