BRIEF REPORT •

Presence of Tissue Transglutaminase IgA Antibody as a Celiac Disease Marker in a Sample of Patients with Irritable Bowel Syndrome

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Recent medical literature agrees that celiac disease (CD) is much more prevalent in western civilization than it was thought to be in the past. Given the potential complications and consequences of untreated CD, screening programs have been considered. Symptoms of celiac disease may resemble those of Irritable Bowel Syndrome. A group of patients with IBS was screened for CE using the Tissue Transglutaminase Antibody IgA serum test. A total of 18 patients were screened. All of our patients tested negative for TTG IgA. This finding may indicate that the prevalence of CD may be low in our population. Further population studies are needed to confirm our finding. [P R Health Sci J 2015;34:38-39]

Key words: Celiac Disease, Irritable Bowel Syndrome, Tissue transglutaminase IgA antibody, Puerto Rico

eliac disease (CD), also known as gluten-sensitive enteropathy, is characterized by intolerance to gluten, rye, wheat, and barley. Diarrhea and malabsorption are 2 classic symptoms of the disease. These symptoms are caused by immune-mediated intestinal mucosal injury. Clinical manifestations of CD tend to differ by age group. Most of the literature agrees that CD is slightly more prevalent in women than in men. Its age distribution is bimodal, with the first peak in infancy and a second in the third to fourth decade of life. Extraintestinal manifestations are more common in adults than in children. These can be related to malabsorption but also may be independent of nutritional status. Malabsorption may cause iron deficiency, peripheral neuropathy, weakness, weight loss, night blindness, muscle cramps, bone demineralization, and bleeding disorders. Extra intestinal manifestations, independent of malabsorption, include dermatitis herpetiformis, neuropsychiatric disease, arthritis, myocarditis, liver dysfunction, lymphoma, glomerular disease, pulmonary hemosiderosis, migraines, depression, and infertility (1-3).

The perspective of CD in the United States has changed over the past decade. Previously, CD prevalence was estimated to be 1 case per 3000 to 6000 persons (1). The disease was thought to be exclusive to the European population, with a prevalence (in that population) of 1 case per 130 to 300 persons (2). However, more recent studies estimate that the prevalence of CD in the United States is closer to 1 case per 133 to 250 persons (1). Given this new epidemiological data, and the potentially severe consequences of untreated CD, the creation of a national screening program has been considered. The prevalence of CD in Puerto Rico has not been established, but studies in Latin America (Argentina and Brazil) identified the prevalence in

that region as being 1 case per 167 to 360 persons (4). This latter study indicates that the prevalence of CD in this Latin America population is very similar to the prevalence seen in the European population.

Aside from ethnic differences, there are certain patient groups that have an increased risk for CD. Patients with irritable bowel syndrome (IBS) very often have symptoms that are similar to those of patients with CD (5–6). Studies designed to address this finding have shown that patients with IBS have a higher prevalence of CD serologic markers than a control population (7). Other studies propose that CD-associated mucosal inflammation may have a sensitizing effect that predisposes certain individuals to IBS-type symptoms (8). These results often vary according to the study-subject sample being evaluated.

Some studies suggest that people with CD have modest increases in overall risk of malignancy, especially small intestinal lymphoma and GI carcinomas (3). It has also been well documented that CD has significant morbidity and a high risk for mortality because of its numerous complications. Therefore, an improvement in screening both to detect prevalence and to establish an early treatment will most likely improve patient survival and quality of life.

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Methods

Given the concern that CD prevalence is rising in western populations, our study group decided to address this issue. A study of patients visiting University of Puerto Rico School of Medicine gastroenterology clinics was conducted. The study investigators identified patients with symptoms suggestive of IBS. These patients were self-referred and were seeking medical attention regarding gastrointestinal complaints. Subjects fulfilling the Rome III criteria (9) for the diagnosis of IBS were invited to participate and, if agreeable, recruited by the investigators. Consent was obtained. Age and sex data were collected. Based on the Rome III criteria, each patient's IBS diagnosis was classified as being one of the following: diarrhea, constipation, mixed, or unsubtype IBS (9). After consent and IBS classification, a tissue transglutaminase IgA test was ordered. Patients were instructed to go to the selected laboratory for blood drawing. A total of 5mL of blood was drawn at Quest Diagnostics, in Hato Rey, PR. Tissue transglutaminase IgA antibody levels were identified by ELISA Immunoassay. Results were reported as negative when the levels were less than 5 U/mL, equivocal when they were from 5 to 8 U/mL, and positive when they were greater than 8 U/mL. This test has a sensitivity of 90% to 96% and a specificity of greater than 95% for identifying CD (10). Sblattero D et al. showed that this test is cost effective for the diagnosis of CD (11). Frequency distributions were computed to describe the demographic and clinical characteristics of the study group. The study was approved by the IRB of the University of Puerto Rico Medical Sciences Campus.

Discussion

A total of 32 patients were diagnosed with IBS. Seven patients were women and 25 were men. The mean age of the participants was 48.5 + 11.5 years. The predominant IBS type was IBS with constipation. The supporting symptoms for IBS were quantified. The majority of patients (31.3%) had 4 supporting symptoms (Table 1). Of our study population, 18 patients underwent serum sampling. Results were negative for tissue transglutaminase IgA antibodies for all 18 patients (100%).

This is the first report of serologic screening for tissue transglutaminase IgA antibodies in patients with IBS living in Puerto Rico. The results are limited by the study's small sample size and should not be interpreted as showing that there is an absence of CD in patients with IBS living in Puerto Rico. Even if we accept a prevalence of 1 case per 133 to 250 persons for the USA (1), or 1 case per 167 to 360 persons for Latin America (4), we would not statistically expect to find a case of CD with our limited testing sample of only 18. Given the potential risks to the patient of untreated CD and based on the current literature, which indicates that there may be a higher prevalence of CD in our hemisphere than has previously been thought to be the case, a larger prospective study should be done to definitively determine the prevalence of CD in Puerto Rico.

Table 1. Symptoms supportive of IBS diagnosis

Number of symptoms*	Number of patients	Percent (N = 32)
2	3	3/32 (9.4%)
3	6	6/32 (18.7%)
4	10	10/32 (31.3%)
5	8	8/32 (25.0%)
6	5	5/32 (16.6%)

*Symptoms include the following: abnormal stool frequency and/or fewer than 3 bowel movements per week; more than 3 bowel movements per week; lumpy/hard stools; loose, watery stool; straining on/urgent defecation.

Resumen

La literatura médica reciente está de acuerdo que la enfermedad celiaca (EC) es mucho mas prevalente en el occidente de lo que se había pensado en un pasado. Dado a las posibles complicaciones y consecuencias de la EC no tratada, se han considerado programas de cernimiento. Se ha descrito que la EC puede presentar síntomas muy parecidos a los del síndrome del intestino irritable. Nuestro grupo tomó muestras a varios pacientes con enfermedad del intestino irritable y se le hizo cernimiento para EC utilizando la prueba de suero transglutaminasa IgA (TTG IgA). Un total de dieciocho pacientes fueron muestreados. Nuestro grupo de pacientes en su totalidad resultó ser negativo para TTG IgA. Este hallazgo pudiese indicar que la prevalencia de la EC es baja en nuestra población. Estudios poblacionales son necesarios para confirmar nuestro hallazgo.

References

- Leffler D, Saha S, Farrell RJ. Celiac Disease. Am J Manag Care 2003;9: 825–831.
- Nelsen DA Jr. Gluten-Sensitive Enteropathy (Celiac Disease): More Common Than You Think. Am Fam Physician 2002;66:2259–2266.
- Green PHR, Stavropoulos SN, Panagi SG, et al. Characteristics of adult celiac disease in the USA: results of a national survey. Am J Gastroenterol 2001;96:126–131.
- Araya QM. Improving the management of celiac disease: an urgent challenge [in Spanish]. Rev Med Chil 2006;134:361–364.
- Wahnschaffe U, Ulrich R, Riecken EO, Schulzke JD. Celiac Disease-like abnormalities in a subgroup of patients with irritable bowel syndrome. Gastroenterology 2001;121:1329–1338.
- Verdu E, Armstrong D, Murray J. Between Celiac Disease and Irritable Bowel Syndrome: The "No Man's Land" of Gluten Sensitivity. Am J Gastroenterol 2009;104:1587–1594.
- Sanders DS, Carter MJ, Hurlstone DP, et al. Association of adult celiac disease with irritable bowel syndrome: a case-control study in patients fulfilling ROME II criteria referred to secondary care. Lancet 2001;358:1504–1508.
- O'Leary C, Wieneke P, Buckley S, et al. Celiac disease and irritable boweltype symptoms. Am J Gastroenterol 2002; 97:1463–1467.
- Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. In: Drossman DA, Corazziari E, Delvaux M, Spiller RC, Talley NJ, Thompson WG, Whitehead WE, eds. Rome III: The Functional Gastrointestinal Disorders, 3rd ed. McLean, VA: Degnon Associates, Inc.; 2006:1480–1491.
- Leffler DA, Schuppan D. Update on serologic testing in celiac disease. Am J Gastroenterol 2010;105:2520–2524.
- 11. Sblattero D, Berti I, Trevisiol C, et al. Human recombinant tissue transglutaminase ELISA: an innovative diagnostic assay for celiac disease. Am J Gastroenterol 2000;95:1253–1257.