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Elevated Celiac Antibodies and Abnormal Duodenal Biopsies Associated with IBD Markers: Possible Role of Altered Gut Permeability and Inflammation in Gluten Related Disorders

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Abstract : Wheat is one of the most commonly consumed grains worldwide, which contains gluten. Nowadays, gluten intake is considered to be a trigger for GRDs, including Celiac disease (CD), a common genetic disease affecting 1% of the US population, non-celiac gluten sensitivity (NCGS) and wheat allergy. NCGS is being recognized as an acquired gluten-sensitive enteropathy that is prevalent across age, ethnic and geographic groups. The cause of this entity is not fully understood, and recent studies suggest that it is more common in participants with irritable bowel syndrome (IBS), with iron deficiency anemia, symptoms of fatigue, and has considerable overlap in symptoms with IBS and Crohn's disease. However, these studies were lacking in availability of complete serologies, imaging tests and/or pan-endoscopy. We performed a prospective study of 745 adult patients who presented to an outpatient clinic for evaluation of chronic upper gastro-intestinal symptoms and subsequently underwent an upper endoscopic (EGD) examination as standard of care. Evaluation comprised of comprehensive celiac antibody panel, inflammatory bowel disease (IBD) serologic markers, duodenal biopsies and Small Bowel Video Capsule Endoscopy (VCE), when available. At least 6 biopsy specimens were obtained from the duodenum and proximal jejunum during EGD, and CD3+ Intraepithelial lymphocytes (IELs) and villous architecture were evaluated by a single experienced pathologist, and VCE was performed by a single experienced gastroenterologist. Of the 745 patients undergoing EGD, 12% (93/745) patients showed elevated CD3+ IELs in the duodenal biopsies. 52% (387/745) completed a comprehensive CD panel and 7.2% (28/387) were positive for at least 1 CD antibody (Tissue transglutaminase (tTG), being the most common antibody in 65% (18/28)). Of these patients, 18% (5/28) showed increased duodenal CD3+ IELs, but 0% showed villous blunting or distortion to meet criteria for CD. Surprisingly, 43% (12/28) were positive for at 1 IBD serology (ASCA, ANCA or expanded IBD panel (LabCorp)). Of these 28 patients, 29% (8/28) underwent a SB VCE, of which 100 % (8/8) showed significant jejuno-ileal mucosal lesions diagnostic for IBD. Findings of abnormal CD antibodies (7.2%, 28/387) and increased CD3+ IELs on duodenal biopsy (12%, 93/745) were observed frequently in patients with UGI symptoms undergoing EGD in an outpatient clinic. None met criteria for CD, and a high proportion (43%, 12/28) showed evidence of overlap with IBD. This suggests a potential causal link of acquired GRDs to underlying inflammation and gut mucosal barrier disruption. Further studies to investigate a role for abnormal antigen presentation of dietary gluten to gut associated lymphoid tissue as a cause are justified. This may explain a high prevalence of GRDs in the population and correlation with IBS, IBD and other gut inflammatory disorders.

Keywords : celiac, gluten sensitive enteropathy, lymphocitic enteritis, IBS, IBD
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