

History of Tonsillectomy Is Associated With Irritable Bowel Syndrome

To the Editor:

Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder characterized by altered bowel function, abdominal discomfort, and bloating^{1,2} affecting 20% of individuals worldwide.^{3,4} The diagnosis is based on specific clinical criteria in the absence of a detectable organic cause.⁵ Interestingly, there is growing literature that patients with IBS have alterations in intestinal microbiota.

The human gut is an elaborate ecosystem composed of 10¹⁴ bacteria established in the first year of life⁶ and continuously altered by exogenous factors; however, genetics significantly contribute as well.^{7,8} The general requirement of intestinal colonization is microbial access to the intestinal tract, counteracted by enzymes, gastric acid, and the mucosal immune system. As microbes enter the human digestive tract, the first major encounter with the host immune system is the tonsils.

The tonsils are important sentinels in the detection of foreign antigens/bacteria entering the digestive tract, and their removal may influence bacterial colonization/invasion of the alimentary tract. We examined whether a history of tonsillectomy is associated with the presence of IBS.

We utilized a prospectively collected dataset of patients referred to a tertiary medical center. Patients with IBS (Rome I criteria) completed a symptom questionnaire to assess bowel

symptoms. Bivariate and multivariate analyses were employed to assess associations between IBS, tonsillectomy, GI symptoms, and demographics.

A total of 1125 patients (72% female), mean age 44.4 ± 17.5 years were evaluated. Of these, 530 patients had IBS. A history of tonsillectomy was observed in 59.5% and 40.5% of patients with and without IBS, respectively ($P = 0.001$). Confounding variables associated with IBS included age and sex; after controlling for age and sex, tonsillectomy was significantly associated with IBS ($P = 0.001$).

This is the first study demonstrating that tonsillectomy is associated with IBS. The rationale for this relationship is unclear, although we have set forth several hypotheses: the health seeking nature of IBS patients⁹ and higher rates of other surgeries¹⁰ may explain the higher rate of tonsillectomy, inflammation of the tonsils. Furthermore, the need for tonsillectomy implies an alteration in the host immune response (also found in IBS patients), and the absence of tonsils may enable successful and undetected pathogen penetration into the intestinal tract leading to postinfectious IBS or even bacterial overgrowth. Further investigation is warranted to understand the novel link between tonsillectomy and IBS.

Robert J. Basseri, MD*

Kelly Chong, PhD†

Christopher Chang, MD, PhD*

Mark Pimentel, MD, FRCP(C)*

*GI Motility Program, Cedars-Sinai Medical Center

†Quality Improvement Resource Center, Veterans Administration Greater, Los Angeles Healthcare System, Los Angeles, CA

REFERENCES

- Manning AP, Thompson WG, Heaton KW, et al. Towards positive diagnosis of the irritable bowel. *BMJ*. 1978;2: 653–654.
- Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. *Gastroenterology*. 2006;130:1480–1491.
- Wilson S, Roberts L, Roalfe A, et al. Prevalence of irritable bowel syndrome: a community survey. *Br J Gen Pract*. 2004;54:494–502.
- Gwee KA, Wee S, Wong ML, et al. The prevalence, symptom characteristics,

and impact of irritable bowel syndrome in an Asian urban community. *Am J Gastroenterol*. 2004;99:924–931.

- Drossman DA, Richter JE, Talley NJ, et al. *Functional Gastrointestinal Disorders: Diagnosis, Pathophysiology and Treatment: A Multinational Consensus*. Boston: Little, Brown; 1994.
- Palmer C, Bik EM, DiGiulio DB, et al. Development of the human infant intestinal microbiota. *PLoS Biol*. 2007;5:e177.
- Ley RE, Turnbaugh PJ, Klein S, et al. Microbial ecology: human gut microbes associated with obesity. *Nature*. 2006; 444:1022–1023.
- Hopkins MJ, Sharp R, MacFarlane GT. Age and disease related changes in intestinal bacterial populations assessed by cell culture, 16S rRNA abundance, and community cellular fatty acid profiles. *Gut*. 2001;48:198–205.
- Longstreth GF, Wilson A, Knight K, et al. Irritable bowel syndrome, health care use, and costs: a U.S. managed care perspective. *Am J Gastroenterol*. 2003; 98:600–607.
- Longstreth GF, Yao JF. Irritable bowel syndrome and surgery: a multivariable analysis. *Gastroenterology*. 2004;126: 1665–1673.

Transient Celiac Autoimmunity in an Adult

To the Editor:

Serological testing offers a convenient and accurate means to screen for celiac disease (CD). The high sensitivity and specificity of tissue transglutaminase (TTG) and endomysial antibodies (EMA) for villous atrophy have resulted in the use of these markers as surrogates for mucosal biopsy in the diagnosis of CD. We report here a case of transient development and complete resolution of celiac antibodies in an adult patient who remained on a gluten-containing diet.

A 58-year-old man, who regularly consumed gluten in concert with his employment in a bagel/sandwich shop, was referred for evaluation of positive celiac serologies. Vitamin D deficiency had prompted celiac testing in March

Dr Green is on the Scientific Advisory Board of Alvine Pharmaceuticals and ImmusanT. The authors declare that they have nothing to disclose.

Dr Robert Basseri, Dr Christopher Chang, and Kelly Chong have no competing interests. Dr Mark Pimentel is a consultant for and has grants from Salix Pharmaceuticals. Cedars-Sinai Medical Center has a licensing agreement with Salix Pharmaceuticals. There are no commercial associations that might pose or create a conflict of interest with information presented in this submitted manuscript such as consultancies, stock ownership, or patent licensing arrangements. All sources of funds supporting the completion of this manuscript are under the auspices of the Cedars-Sinai Medical Center.

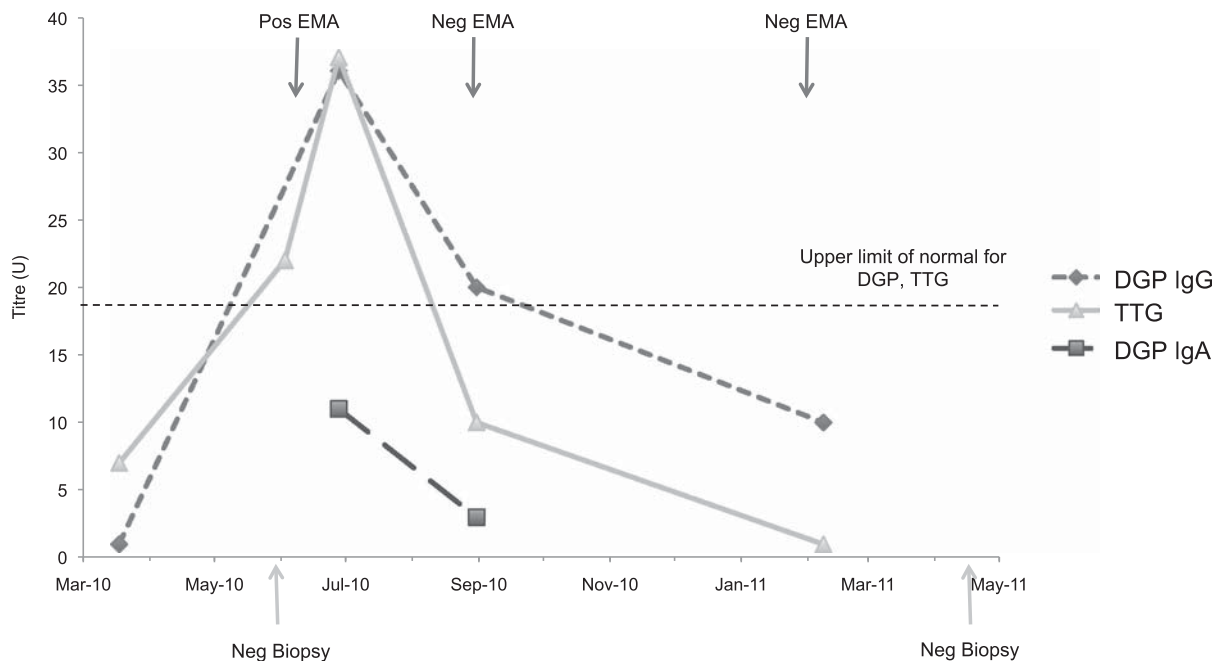


FIGURE 1. Serology and biopsy timeline. DGP indicates deamidated gliadin peptide; EMA, endomysial antibody; TTG, tissue transglutaminase.

2010. His α -TTG and α -deamidated gliadin peptide (DGP) antibodies were within the normal range and small bowel biopsies obtained on endoscopy for esophageal reflux were normal. Two months later, however, repeat serology performed for workup of secondary hyperparathyroidism revealed the development of a positive α -TTG titer of 22 units and a positive α -EMA of 1:40. Confirmatory tests again demonstrated positive TTG and IgG DGP antibodies at 37 and 36 units, respectively. The patient was found to be human leukocyte antigen-DQ2-positive. TTG and EMA drawn in September 2010 had resolved, with only IgG DGP remaining weakly positive. All 3 antibodies subsequently normalized by February. Repeat upper endoscopy and biopsy in April 2011 for ongoing reflux revealed well formed villi in the duodenal bulb and descending duodenum, with patchy mild intraepithelial lymphocytosis restricted to the villous tips, a pattern described in patients with latent or potential CD.¹

This patient demonstrated development and subsequent resolution of TTG, EMA, and DGP antibodies over a time frame of several months, with ongoing gluten consumption. We believe this to be the first documented adult case of transient seroconversion with reversion to normal of all celiac antibodies similar to the phenomenon documented in children at-risk for CD.²

Transient celiac autoimmunity has significant implications for the validity of seroprevalence studies that use TTG and EMA to estimate CD prevalence without confirmatory biopsy.^{3,4} In addition, transient celiac or gluten autoimmunity could account for a significant proportion of “false positive” antibody tests in which the timing of serology and biopsy (Fig. 1) does not coincide. This case illustrates the crucial importance of duodenal biopsy and close follow-up of those with normal biopsy results despite abnormal serologic findings. Temporary celiac autoimmunity can occur in adults, and further studies examining

the natural history of celiac antibodies in adults are warranted.

Srihari Mahadev, MBBS

Govind Bhagat, MD

Peter H. R. Green, MD

Celiac Disease Center, Columbia University
College of Physicians and Surgeons
New York, NY

REFERENCES

- Järvinen TT, Collin P, Rasmussen M, et al. Villous tip intraepithelial lymphocytes as markers of early-stage coeliac disease. *Scand J Gastroenterol.* 2004;39:428–433.
- Simell S, Hoppu S, Hekkala A, et al. Fate of five celiac disease-associated antibodies during normal diet in genetically at-risk children observed from birth in a natural history study. *Am J Gastroenterol.* 2007;102:2026–2035.
- Rubio-Tapia A, Kyle RA, Kaplan EL, et al. Increased prevalence and mortality in undiagnosed celiac disease. *Gastroenterology.* 2009;137:88–93.
- West J, Logan RF, Hill PG, et al. Seroprevalence, correlates, and characteristics of undetected coeliac disease in England. *Gut.* 2003;52:960–965.