Celiac Disease Refractory to a Gluten-free Diet?

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CASE DESCRIPTION

A 75-year-old woman from an outside hospital was referred because of continued signs and symptoms of celiac disease (gluten-sensitive enteropathy) that persisted despite self-reported adherence to a gluten-free diet. The patient reported excessive gas, bowel distension, a 15-pound weight loss over the past few years, insomnia, and a rash over her lower extremities. The patient had required hospitalizations, intravenous fluids, and continuing therapy with corticosteroids for 6 months.

A diagnosis of celiac disease had been made 6 years previously, based on (*a*) typical gastrointestinal signs and symptoms with negative stool cultures and *Clostridium difficile* toxin assay, (*b*) positive serology for celiac disease, (*c*) unremarkable colonoscopy with normal random biopsy results, and (*d*) small-bowel biopsy results showing evidence of villous blunting with increased chronic inflammatory cells. At that time, the patient's laboratory results included antigliadin antibody (AGA) IgG 0.8 AU (<10 AU), anti-AGA IgA 1.1 AU (<5 AU), anti–tissue transglutaminase (tTG) IgA 9.2 AU (<4 AU), and normal total IgA and IgA antiendomysial antibody (EMA) values. A computed tomographic scan was negative for lymphoma, and an upper gastrointestinal series and small-bowel follow-through barium x-ray were normal. Endoscopic biopsy results obtained during the previous 2 years showed continued villous atrophy with intraepithelial lymphocytes. Shortly before the patient's referral, repeat biopsies showed villous blunting with increased chronic inflammation, findings confirmed by a gastrointestinal pathologist at our institution.

The patient, a pleasant, frail-looking, elderly woman in no acute distress, was retired and married with 2 adult children. She denied smoking and alcohol use and had no family history of celiac disease, liver disease, or colon cancer. Her medical history was remarkable for placement of a carotid artery stent 5 years earlier. Physical examination was unremarkable except for the presence of a maculopapular rash inconsistent with dermatitis herpetiformis and with dependent distribution over the lower legs.

The patient's blood pressure was 133/59 mmHg, pulse 51 beats/min, temperature 36.5 °C, and weight 59.4 kg. Laboratory results since her referral included vitamin B_{12} 245 ng/L

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[reference interval (RI), 251–911 ng/L], iron 370 μg/L (RI, 400–1450 μg/L), anti-tTG IgA 13 AU (RI, 0–20 AU), and 5'nucleotidase 22.1 U/L (RI, 4.0–11.5 U/L).

The patient met with a nutritionist and implemented recommended dietary changes to eliminate gluten. Her symptoms temporarily improved, with a return to normal bowel function, but after a short time her symptoms recurred. Results of further tests excluded conditions known to complicate or coexist with celiac disease, including bacterial overgrowth, microscopic colitis, and lactose intolerance. Because the patient's symptoms were refractory to treatment and required prolonged, continued use of corticosteroid therapy, esophagogastroduodenoscopy with duodenal biopsies was performed, and formalin-fixed small-bowel biopsy tissue samples were sent to the molecular diagnostic laboratory for additional testing.

Questions to Consider
• What is gluten and which foods contain gluten?
• What laboratory tests can be performed to support a diagnosis of celiac disease?
• What are the possible explanations for persistence of symptoms of celiac disease despite apparent adherence to a gluten-free diet?
• What molecular test was performed and how can this aid in the diagnosis?

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the February 2008 issue of *Clinical Chemistry* in approximately 3-4 weeks. To view the case and comments online, go to http://www.clinchem.org/content/vol54/issue2/ and follow the link to the Clinical Case Studies.

Educational Centers

If you are associated with an educational center and would like to receive the cases and questions 3-4 weeks in advance of publication, please email clinchem@aacc.org.

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