

Iron-deficiency anemia due to silent celiac sprue

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Celiac sprue, a gluten-induced enteropathy, was once considered primarily an immunologic disease of infants and children. Gluten is a protein found in grains, primarily wheat and barley. The ingestion of gliadin, a component of gluten, causes gastrointestinal symptoms including malabsorption and multiple nutritional deficiencies. Our understanding of this disorder has become more refined in recent years, as the case studies demonstrate.

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Case 1: A 14-year-old male student presented for a routine athletic physical examination. He reported no cardiovascular or gastrointestinal symptoms and had gained weight. His examination was normal; however, his blood hemoglobin was 11.6 g/dL, with microcytic red blood cells and a ferritin level of 5 ng/mL. Upper and lower endoscopic findings were macroscopically normal. Biopsy of the proximal duodenum showed villous atrophy and lymphocytic infiltrate in the lamina propria. Subsequent serologic studies revealed an anti-immunoglobulin A (IgA) tissue-transglutaminase antibody level of 6.88 units (normal is <1.0), and the anti-IgA endomysial antibody titer was positive (1:640). A gluten-free diet was instituted, and after 1 year the blood hemoglobin was 15.7 g/dL with restoration of ferritin and all serologic levels to normal. The student remains without symptoms and plays linebacker on his varsity football team.

Case 2: In 1992, a 41-year-old woman, referred by her gynecologist, presented with a blood hemoglobin of 6.7 g/dL. She was on hormone replacement therapy with no menstrual bleeding. Her ferritin was unmeasurable. The patient denied any symptoms or weight loss, and except for pallor, her examination results were normal. Iron repletion with oral elixir increased her blood hemoglobin to 12 g/dL in 1 year, without elevation of the ferritin. In November 2000, a bone mineral density study revealed severe osteoporosis requiring therapy with alendronate. She remained asymptomatic. Serologic studies for celiac sprue were obtained. The anti-IgA tissue transglutaminase antibody level was 5.1 units. The anti-IgA endomysial antibody titer was positive (1:320). After 5 months on a gluten-free diet, her study results returned to normal and she remained without symptoms.

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In recent decades, the pathophysiology of celiac sprue has been clarified. Environmental, immunologic, and genetic factors are responsible for the histologic findings of flattening and atrophy of the small intestinal mucosal villi, crypt elongation, and lymphoid proliferation in the lamina propria. These changes may

account for decreased levels of disaccharidase, alkaline phosphatase, and hydrolases, predisposing patients to lactose intolerance and other functional defects in the intestinal mucosa. This condition requires the antigenic stimulus of gluten in the small intestine, causing formation of IgA antibodies directed against gliadin and tissue transglutaminase. When detected, these antibodies are 90% to 95% sensitive and specific for celiac sprue (1). Individuals sharing these findings are usually of European descent; the prevalence of the condition is 1 per 300 of the general white population. Evidence exists for possible dominant inheritance with incomplete expression of the genetic influence. There is a female predominance, and the incidence is higher in HLA-DQ2 phenotypes.

Signs and symptoms may occur from infancy to the eighth decade of life. Fewer than half of affected patients complain of diarrhea. In an Italian study of 252 celiac sprue patients, only 43% displayed classic gastrointestinal symptoms. The symptomatic patient may have steatorrhea with malabsorption syndrome or selected deficiencies of iron, folate, or protein. Clinical manifestations include refractory anemia, osteoporosis, dermatitis herpetiformis, or neurologic signs. A feared complication in untreated disease is intestinal lymphoma (2, 3).

Celiac sprue is definitively diagnosed by small intestinal biopsy, but the serologic test for IgA antibody against tissue transglutaminase is extremely accurate. This test has replaced the older test for the IgA antibody against endomysial antigen, which may be absent even in severe disease (4). Due to the requirement for strict dietary compliance, many experts advocate small bowel biopsy before initiation of the gluten-free diet.

Interesting associations link celiac sprue with other immunologic conditions including insulin-dependent diabetes mellitus, autoimmune thyroid disease, and IgA deficiency (5). Celiac sprue is treated with a strict lifelong avoidance of grains containing gluten. There are many sources of "hidden gluten," including fillers in toothpaste, certain patent medications, deodorants, cosmetics, seasonings, and any grain-fermented alcohol. Even microscopic amounts of gluten may trigger intestinal reactions. Symptoms and histologic and serologic findings return to normal in a matter of months in patients who comply with the diet (6).

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The diagnosis of celiac sprue should be considered in any patient presenting with unexpected or unexplained deficiencies of iron, folate, or other elements, or with nonspecific gastrointestinal complaints undiagnosed by conventional studies. The high prevalence in the general population and the grave consequences of misdiagnosis make celiac sprue a significant health hazard.

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Celiac sprue dietary resources include the following:

- www.csaceliacs.org (Celiac Sprue Association/USA)
- www.foodallergies.com
- www.celiac.com