

## CLINICAL VIGNETTE

### Celiac Disease

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#### **Case Report**

A 41-year-old woman was referred by her gynecologist for a blood hemoglobin of 6.7 g/dL. She was on hormone replacement therapy with no menstrual bleeding. The patient denied any symptoms or weight loss, and except for pallor, her physical examination was normal. Her red blood cell indices were microcytic and her ferritin was unmeasurable. Iron repletion with oral elixir increased her hemoglobin to 12 g/dL, without elevation of the ferritin. A bone mineral density study revealed severe osteoporosis and she was started on alendronate. 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.

#### **Discussion**

Celiac disease, also referred to as celiac sprue, gluten-sensitive enteropathy, and non-tropical sprue, is a small bowel malabsorption disorder that results in mucosal inflammation, villous atrophy, and crypt hyperplasia, which occur on exposure to gluten,<sup>1</sup> the water insoluble protein commonly found in wheat, rye, and barley. It is an autoimmune disorder of the small bowel, resulting from T cell activation that is triggered by chronic exposure to the gliadin component of gluten in genetically predisposed persons.<sup>2</sup> The mucosal changes of celiac disease occur over months to years.<sup>2</sup>

The prevalence of celiac disease is difficult to estimate because of its variable presentation.<sup>1</sup> The prevalence has increased largely because of the development of serologic markers for celiac disease.<sup>3</sup> Persons of all ages are affected, although celiac disease presents most commonly in either early childhood or between the third and fourth decades of life.<sup>4</sup> The female-to-male ratio in adulthood is 2:1.<sup>2</sup> The disease occurs most often in Celtic populations and is rare in persons of Chinese, Japanese or Afro-Caribbean descent.<sup>1</sup> The data suggest that celiac

disease has a 1% prevalence in the general population.<sup>1</sup>

Celiac disease has a strong hereditary component. The prevalence of the condition in first-degree relatives is approximately 10% and there is more than 70% concordance in identical twins.<sup>2</sup> Strong association exists between celiac disease and 2 human leukocyte antigen (HLA) haplotypes (DR3 and DQw2).

#### **Clinical Features and Diagnosis**

The diagnosis of celiac disease can be easily missed. Gastrointestinal symptoms are frequent but nongastrointestinal features are common as well.<sup>3</sup> Severe cases of celiac disease may present with the classic textbook symptoms of diarrhea, steatorrhea, weight loss, fatigue and iron deficiency anemia.<sup>3</sup> Most patients have milder symptoms. In fact, there is a trend toward a decreasing number of patients presenting with diarrhea and an increasing number presenting with anemia and osteoporosis.<sup>5</sup>

Less common features of celiac disease include short stature, delayed puberty, recurrent aphthous stomatitis, folate deficiency, osteopenia or osteoporosis, dental enamel hypoplasia, thrombocytosis (hypersplenism), infertility, polyneuropathy, arthralgia, anxiety and depression, hypocholesterolemia and low HDL.<sup>2</sup>

Celiac disease is also associated with certain conditions. Seventy-five percent of adults with dermatitis herpetiformis have celiac disease on duodenal biopsy.<sup>3</sup> The skin lesions respond to a gluten-free diet. The lesions are associated with severe pruritus, erythematous blisters that are symmetric in distribution on the face, elbows, back buttocks and knees.<sup>3</sup> Five percent of celiac patients have dermatitis herpetiformis and it is not commonly seen in children with celiac disease.<sup>3</sup> Other associated conditions are Type 1 diabetes, autoimmune thyroid disease, IgA nephropathy, Down syndrome and rheumatoid arthritis.<sup>2</sup>

Celiac patients may have an increased risk of gastrointestinal malignancies and intestinal lymphoma. Several studies suggest that adherence to a gluten-free diet reduces the risk of lymphoma in patients with celiac disease.<sup>1</sup>

A thorough history and physical examination is neces-

sary. Laboratory tests should include a complete blood count, ferritin, iron studies, folate levels, albumin, and carotene. In patients with chronic diarrhea, stool should be examined for fecal fat. A 72-hour fecal fat collection may be helpful in quantitating steatorrhea. Stool should also be sent for ova and parasites, giardia and *Clostridium difficile*.<sup>2</sup>

Serologic testing is extremely helpful in making the diagnosis of celiac disease, but a histologic diagnosis based on duodenal or jejunal pathology and the response to a gluten-free diet are the gold standard.<sup>2</sup> Histopathologic examination of a biopsy specimen shows villous atrophy, crypt hyperplasia and infiltration of the lamina propria with lymphocytes.<sup>3</sup> Typical endoscopic findings in celiac disease include mucosal atrophy, fissuring and scalloping. Gross mucosal signs are only 50% sensitive compared with histologic assessment. Appropriate sampling of at least 6 biopsies from non-bulbar duodenum should be taken.<sup>2</sup>

Although celiac sprue is definitively diagnosed by small intestinal biopsy, serologic tests are helpful as well. Antigliadin IgG and IgA, antiendomysial IgA, anti-tissue transglutaminase IgA and total IgA are the most common serologic markers for celiac disease.<sup>1</sup> The sensitivity of IgA anti-gliadin antibodies is reported to range from 70% to 85%; the specificity ranges from 70% to 90%.<sup>1</sup> IgA antiendomysial and anti-tissue transglutaminase antibodies have sensitivities that exceed 90% and specificities of more than 95%.<sup>1</sup> Serological analysis for IgA antitissue transglutaminase is the most widely used test to help diagnose celiac sprue; however, 3% to 5% of all patients with celiac disease are IgA deficient. Therefore, determining total IgA prior to antibody testing is appropriate in patients with celiac disease.<sup>2</sup>

The presence of serum IgA antibody to endomysium in untreated celiac sprue has higher sensitivity and higher specificity than antigliadin antibodies; however, serum IgA antiendomysial antibody often becomes undetectable after 6 to 12 months of gluten withdrawal.<sup>1</sup> In a patient with a high clinical likelihood of celiac disease, negative results on serologic testing do not rule out the diagnosis and duodenal biopsies must be performed.<sup>2</sup>

### **Treatment**

Treatment of celiac disease consists of strict adherence to a gluten-free diet.<sup>2</sup> Complete histologic and

symptomatic resolution of the disease occurs when products that contain wheat, barley and rye are avoided.<sup>3</sup> Adherence to a gluten-free diet has been shown to improve bone mineral density, iron deficiency anemia and nutritional status.<sup>1</sup>

Historically, there was some concern that oats may not be safe in celiac disease.<sup>1</sup> Some studies have shown no adverse effects in patients with celiac disease.<sup>4</sup> There is some concern that oats can become contaminated with wheat in the milling process.<sup>3</sup> A gluten-free diet is effective but challenging for patients with celiac disease because of the centrality of grains to the Western diet and the presence of gluten in processed foods.<sup>2</sup> Consultation with nutritionists and the American Celiac Society is important.

If a patient does not respond to a gluten-free diet within 3 months, the most likely cause is continued gluten exposure from hidden sources or noncompliance.<sup>2</sup> Compliance can be monitored by checking an IgA antigliadin antibody level. This number should fall in patients adhering to a gluten-free diet.<sup>3</sup> A small percentage of patients with celiac disease fail to respond to a gluten-free diet. In some patients who are refractory, corticosteroids might be helpful.<sup>2</sup>

Patients with celiac disease should be given iron, folate and calcium repletion, and should also be screened for associated disorders such as thyroid disease, diabetes mellitus and osteoporosis.<sup>2</sup>

Most experts do not recommend screening of asymptomatic persons except for first-degree relatives of persons with celiac disease.<sup>2</sup> Practitioners should consider celiac disease in the differential when patients present with gastrointestinal symptoms, anemia, fatigue and premature osteoporosis.<sup>2</sup>

### **REFERENCES**

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