SMALL BOWEL DISEASES

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MALABSORPTION

The term "malabsorption" denotes disorders in which there is a disruption of digestion and nutrient absorption.

The clinical and laboratory manifestations of malabsorption are summarized in Table 15-11.

1. Celiac Disease

- Typical symptoms: weight loss, chronic diarrhea, abdominal distention, growth retardation.
- Atypical symptoms: dermatitis herpetiformis, iron deficiency anemia, osteoporosis.
- Abnormal serologic test results.
- Abnormal small bowel biopsy.
- Clinical improvement on gluten-free diet.

General Considerations

Celiac disease (also called sprue, celiac sprue, and gluten enteropathy) is a permanent dietary disorder caused by an immunologic response to gluten, a storage protein found in certain grains, that results in diffuse damage to the proximal small intestinal mucosa with malabsorption of nutrients.

Although symptoms may manifest between 6 months and 24 months of age after the introduction of weaning foods, the majority of cases present in childhood or adulthood.

Population screening with serologic tests suggests that the disease is present in 1 : 1 00 whites of Northern European ancestry, in whom a clinical diagnosis of celiac disease is made in only 10%, suggesting that most cases are undiagnosed or asymptomatic. Celiac disease only develops in people with the HLA-DQ2 (95%) or -DQS (5%) class II molecules, which are present in 40% of the population.

Although the precise pathogenesis is unclear, celiac disease arises in a small subset of genetically susceptible (-DQ2 or -DQS) individuals when dietary gluten stimulates an inappropriate immunologic response.

Clinical Findings

The most important step in diagnosing celiac disease is to consider the diagnosis. Symptoms are present for more than 10 years in most adults before the correct diagnosis is established. Because of its protean manifestations, celiac disease is grossly underdiagnosed in the adult population.

A. Symptoms and Signs

The gastrointestinal symptoms and signs of celiac disease depend on the length of small intestine involved and the patient's age when the disease presents. "Classic" symptoms of malabsorption, including diarrhea, steatorrhea, weight loss, abdominal distention, weakness, muscle wasting, or growth retardation, more commonly present in infants (younger than 2 years) . Older children and adults are less likely to manifest signs of serious malabsorption. They may report chronic diarrhea, dyspepsia, or flatulence due to colonic bacterial digestion of malabsorbed nutrients, but the severity of weight loss is variable. Many adults have minimal or no gastrointestinal symptoms but present with extraintestinal "atypical" manifestations, including fatigue, depression, iron deficiency anemia, osteoporosis, short stature, delayed puberty, amenorrhea, or reduced fertility. Approximately 40% of patients with positive serologic tests consistent with disease have no symptoms of disease; the natural history of these patients with "silent" disease is unclear.

Physical examination may be normal in mild cases or may reveal signs of malabsorption such as loss of muscle mass or subcutaneous fat, pallor due to anemia, easy bruising due to vitamin K deficiency, hyperkeratosis due to vitamin A deficiency, bone pain due to osteomalacia, or neurologic signs (peripheral neuropathy, ataxia) due to vitamin B 12 or vitamin E deficiency (Table 15-11) . Abdominal examination may reveal distention with hyperactive bowel sounds.

Dermatitis herpetiformis is regarded as a cutaneous variant of celiac disease. It is a characteristic skin rash consisting of pruritic papulovesicles over the extensor surfaces of the extremities and over the trunk, scalp, and neck.

Dermatitis herpetiformis occurs in less than 1 0 % of patients with celiac disease; however, almost all patients who present with dermatitis herpetiformis have evidence of celiac disease on intestinal mucosal biopsy, though it may not be clinically evident.

B. Laboratory Findings

1. Routine laboratory tests-Depending on the severity of illness and the extent of intestinal involvement, nonspecific laboratory abnormalities may be present that may raise the suspicion of malabsorption and celiac disease (Table 15-11). Limited proximal involvement may result only in microcytic anemia due to iron deficiency. Up to 5% of adults with iron deficiency not due to gastrointestinal blood loss have undiagnosed celiac disease. More extensive involvement results in a megaloblastic anemia due to folate or vitamin B 12 deficiency. Low serum calcium or elevated alkaline phosphatase may reflect impaired calcium or vitamin D absorption with osteomalacia or osteoporosis. Dualenergy x-ray densitometry scanning is recommended for all patients with sprue to screen for osteoporosis. Elevations of prothrombin time, or decreased vitamin A or D levels reflect impaired fat-soluble vitamin absorption. A low serum albumin may reflect small intestine protein loss or poor nutrition. Other deficiencies may include zinc and vitamin B6. Mild elevations of aminotransferases are found in up to 40%.

2. Serologic tests-Serologic tests should be performed in all patients in whom there is a suspicion of celiac disease. The recommended test is the IgA tissue transglutaminase (IgA tTG) antibody, which has a 95% sensitivity and 95% specificity for the diagnosis of celiac disease. Antigliadin antibodies are not recommended because of their lower sensitivity and specificity. IgA antiendomysial antibodies are no longer recommended due to the lack of standardization among laboratories. An IgA level should be obtained in patients with a negative IgA tTG antibody when celiac disease is strongly suspected because up to 3% of patients with celiac disease have IgA deficiency. A test that measures IgG antibodies to deamidated gliadin peptides (anti-DGP) has excellent sensitivity and specificity and is useful in patients with IgA deficiency and young children. Levels of all antibodies become undetectable after 3 - 1 2 months of dietary gluten withdrawal and may be used to monitor dietary compliance, especially in patients whose symptoms fail to resolve after institution of a gluten-free diet.

C. Mucosal Biopsy - Endoscopic mucosal biopsy of the proximal duodenum

(bulb) and distal duodenum is the standard method for confirmation of the diagnosis in patients with a positive serologic test for celiac disease. Mucosal biopsy should also be pursued in patients with negative serologies when symptoms and laboratory studies are strongly suggestive of celiac disease. At endoscopy, atrophy or scalloping of the duodenal folds may be observed. Histology reveals abnormalities ranging from intraepithelial lymphocytosis alone to extensive infiltration of the lamina propria with lymphocytes and plasma cells with hypertrophy of the intestinal crypts and blunting or complete loss of intestinal villi. An adequate normal biopsy excludes the diagnosis. Partial or complete reversion of these abnormalities occurs within 3-24 months after a patient is placed on a gluten-free diet, but symptom resolution remains incomplete in 30% of patients. If a patient with a compatible biopsy demonstrates prompt clinical improvement on a gluten-free diet and a decrease in serologic markers, a repeat biopsy is unnecessary.

..... **Differential Diagnosis**

Many patients with chronic diarrhea or flatulence are erroneously diagnosed as having irritable bowel syndrome. Celiac sprue must be distinguished from other causes of malabsorption, as outlined above. Severe panmalabsorption of multiple nutrients is almost always caused by mucosal disease. The histologic appearance of celiac sprue may resemble other mucosal diseases such as tropical sprue, bacterial overgrowth, cow's milk intolerance, viral gastroenteritis, eosinophilic gastroenteritis, and mucosal damage caused by acid hypersecretion associated with gastrinoma. Documentation of clinical response to gluten withdrawaltherefore is essential to the diagnosis. Some patients complain of symptoms after gluten ingestion but do not have serologic or histologic evidence of celiac disease. The frequency and cause of this entity is debated. A large 2013 study found that symptoms improved in gluten-sensitive patients when placed on a FODMAP restricted diet and worsened to similar degrees when challenged in a double-blind crossover trial with gluten or whey proteins. These data suggest that nonceliac gluten sensitivity may not be a true entity and that the symptom improvement reported by patients with gluten restriction may be due to broader FODMAP elimination.

.... **Treatment**

Removal of all gluten from the diet is essential to therapy all wheat, rye, and barley must be eliminated. Although oats appear to be safe for many patients, commercial products may be contaminated with wheat or barley during processing. Because of the pervasive use of gluten products in manufactured foods and additives, in medications, and by restaurants, it is imperative that patients and their families confer with a knowledgeable dietitian to comply satisfactorily with this lifelong diet. Several excellent dietary guides and patient support groups are available. Most patients with celiac disease also have lactose intolerance either temporarily or permanently and should avoid dairy products until the intestinal symptoms have improved on the gluten-free diet. Dietary supplements (folate, iron, zinc, calcium, and vitamins A, B6, B12, D, and E) should be provided in the initial stages of therapy but usually are not required long-term with a gluten-free diet. Patients with confirmed osteoporosis may require long-term calcium, vitamin D, and bisphosphonate therapy. Improvement in symptoms should be evident within a few weeks on the gluten-free diet. The most common reason for treatment failure is incomplete removal of gluten. Intentional or unintentional re-challenge with gluten may trigger acute severe diarrhea with dehydration, electrolyte imbalance, and may require TPN and intravenous or oral corticosteroids (prednisone 40 mg or budesonide 9 mg) for 2 or more weeks as a gluten-free diet is re-initiated.

..... Prognosis & Complications

If appropriately diagnosed and treated, patients with celiac disease have an excellent prognosis. Celiac disease may be associated with other autoimmune disorders, including Addison disease, Graves disease, type 1 diabetes mellitus, myasthenia gravis, scleroderma, Sjogren syndrome, atrophic gastritis, and pancreatic insufficiency. In some patients, celiac disease may evolve and become refractory to the gluten-free diet. The most common cause is intentional or unintentional dietary noncompliance, which may be suggested by positive serologic tests. Celiac disease that is truly refractory to gluten withdrawal occurs in less than 5% and generally carries a poor prognosis. There are two types of refractory disease, which are distinguished by their intraepithelial lymphocyte phenotype. This diagnosis should be considered in patients previously responsive to the gluten-free diet in whom new weight loss, abdominal pain, and malabsorption develop.

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Table 15-11. Clinical manifestations and laboratory findings in malabsorption of various nutrients.

MANIFESTATIONS	LABORATORY FINDINGS	MALABSORBED NUTRIENTS
Steatorrhea (bulky, light-colored stools)	Increased fecal fat; decreased serum cholesterol; decreased serum carotene, vitamin A, vitamin D	Triglycerides, fatty acids, phospholipids, cholesterol. Fat soluble vitamins: A, D, E, K
Diarrhea (increased fecal water)	Increased stool volume and weight; increased fecal fat; increased stool osmolality gap	Fats, carbohydrates
Weight loss; muscle wasting	Increased fecal fat; decreased carbohydrate (D-xylose) absorption	Fat, protein, carbohydrates
Microcytic anemia	low serum iron	Iron
Macrocytic anemia	Decreased serum vitamin B12 or red blood cell folate	Vitamin B12 or folic acid
Paresthesia; tetany; positive Trousseau and Chvostek signs	Decreased serum calcium or magnesium	Calcium, vitamin D, magnesium
Bone pain; pathologic fractures; skeletal deformities	Osteopenia on radiograph; osteoporosis (adults); osteomalacia (children)	Calcium, vitamin D
Bleeding tendency (ecchymoses, epistaxis)	Prolonged prothrombin time or I.N.R.	Vitamin K
Edema	Decreased serum total protein and albumin; increased fecal loss of alpha-1-antitrypsin	Protein
Milk intolerance (cramps, bloating, diarrhea)	Abnormal lactose tolerance test	Lactose

I.N.R. - international normalized ratio.