Celiac Disease In Infants

Description/Etiology
Celiac disease (CD; also called celiac sprue and gluten-sensitive enteropathy) is a chronic autoimmune disease triggered by ingestion of foods that contain gluten (i.e., a protein found in wheat, rye, and barley); immunoglobulin A (IgA) antibodies to tissue transglutaminase (tTG-IgA) and endomysium (EMA-IgA) are the primary autoantigens. In patients with CD, gluten consumption induces an inappropriate immune response that causes chronic inflammation of the small intestine and villus atrophy with resultant diarrhea and nutrient malabsorption. CD is a multisystem disease with central nervous system (CNS), skin, joint, and reproductive manifestations (for more information, see the series of Quick Lessons on celiac disease). CD has four histologic stages: type 0 (preinfiltrative or normal), type 1 (infiltrative, with increased intraepithelial lymphocytes), type 2 (hyperplastic, type 1 plus crypt [i.e., secretory glands] hyperplasia), and type 3 (destructive, type 2 plus progressively worse villus atrophy).

Although exact etiology is unknown, CD develops in individuals who carry the human leukocyte antigen (HLA) DQ2 or DQ8 haplotype. Genetic susceptibility accounts for approximately 40% of the risk for CD; environmental factors (e.g., age at gluten introduction, length of breast feeding, infections during infancy) account for the remainder.

CD is often diagnosed in infants who develop signs/symptoms (S/S) after cereal is introduced to the diet. In symptomatic infants, the first step is serologic testing for tTG-IgA and total IgA followed by duodenal biopsy (≥ 4 samples) if tTG-IgA is elevated but < 10 times the upper limit of normal (ULN; assay-dependent). If tTG-IgA is > 10 times ULN, EMA-IgA assay and HLA typing is done; if both are positive, duodenal biopsy is unnecessary (Murch et al., 2013). Differential diagnoses include inflammatory bowel disease, other protein intolerance, pediatric irritable bowel syndrome, cystic fibrosis, and autoimmune enteropathy.

Strict lifelong adherence to a completely gluten-free diet (GFD; i.e., no wheat, rye, or barley) is the only treatment; symptoms usually resolve within 3–4 weeks of GFD initiation. Vitamin/mineral supplementation (particularly vitamin B12, folic acid, and iron) might be necessary. Parent/family education about dietary restrictions, emotional support for stress secondary to the diagnosis and dietary restrictions, and continued medical surveillance is essential. Prognosis is excellent; unrelieved S/S are usually secondary to poor GFD adherence.

Facts and Figures
Worldwide, an estimated 1% of the general population has some degree of CD; higher rates are documented in Sweden (~ 2%) and among the Sahrawi of northwestern Africa (~5%). Only 10–15% of patients are diagnosed and treated. Female: male ratio is 1.5–3:1. CD can occur at any age; infants are usually diagnosed at 9–18 months of age.

Risk Factors
Homozygosity (i.e., two copies) for HLA DR3–DQ2 conferred the highest risk for CD at the earliest age; 26% of these children had positive tTG-IgA titers by 5 years of age compared with 2–11% in children with other haplotypes (Liu et al., 2014). Other possible risk factors include age at gluten introduction, duration of breast feeding, infectious disease during...
infancy, and a first-degree relative with type 1 diabetes mellitus (DM1) or CD. CD is also more common in patients with Down, Turner, or Williams syndrome.

### Signs and Symptoms/Clinical Presentation
Abdominal pain, chronic or intermittent diarrhea, and chronic constipation are the most common presenting S/S. Other gastrointestinal (GI) symptoms include anorexia, vomiting, and abdominal bloating. Non-GI S/S can include weight loss or failure to thrive, muscle wasting, seizures, dental enamel hypoplasia, and dermatitis herpetiformis.

### Nutritional Assessment

› **Patient Medical History**
  - Take a complete medical history; ask the patient’s family about the following:
    - The presence of medical conditions (e.g., DM1, GI infections) that can complicate successfully following a GFD
    - The presence of signs and symptoms (e.g., vomiting/diarrhea/constipation, lethargy) that can indicate inadequate intake of nutrients or fluid and reduce appetite
    - Recent unexpected weight loss
    - Family history of CD or other autoimmune diseases (e.g. DM1, Hashimoto’s thyroiditis)

› **Physical Findings of Particular Interest**
  - Abdominal distention and hyperactive bowel sounds might be present
  - Patients with subclinical CD can appear asymptomatic, but serologic tests and villi sampling are positive for CD
  - Patients with CD may show signs of malabsorption (e.g., pallor, muscle wasting, easy bruising)

› **Patient Dietary History**
  - Conduct a diet analysis by asking the patient’s family to complete a diet history (specifically assess for breastfeeding duration, age at gluten introduction, adequate nutrient intake, and consumption of gluten-containing foods)
    - Useful tools for evaluating the patient’s dietary strengths and weaknesses include a food frequency questionnaire and a 3-day diet recall (i.e., patient’s family’s recall of all foods and beverages consumed in a 3-day period that includes 1 weekend day)
  - Ask about accessibility to gluten-free foods
  - Assess for family anxiety and/or depression about the infant’s recently diagnosed CD
    - Ask about the availability of family/social support

› **Anthropometric Data**
  - The Centers for Disease Control and Prevention (CDC) has established references for weight and growth patterns, which can be tracked on weight-for-age/height-for-age/weight-for-height age-based growth charts

› **Laboratory Tests and Diagnostic Tests of Particular Interest to the Nutritionist**
  - Although testing for the EMA-IgA and IgA-TTG antibodies is highly specific and sensitive for CD, testing is not reliable in children < 5 years of age
  - Histologic examination of biopsied small bowel tissue can reveal lymphocytic infiltration, villus atrophy, and mucosal flattening
  - CBC with Hgb and Hct will identify anemia and/or malnutrition, if present
  - Blood tests may be ordered to evaluate for malabsorption; low levels of iron, folate, calcium, and fat-soluble vitamins (A, D, E, and K) may indicate CD

### Treatment Goals

› **Relieve CD Manifestations and Promote Optimal Nutritional Status**
  - Monitor vital signs, assess all physiologic systems (especially the GI system) for manifestations and complications of gluten exposure and poor nutritional intake, and review results of lab tests; immediately report abnormalities to the treating clinician
  - Evaluate for GI discomfort (e.g., nausea/vomiting/diarrhea/constipation) and adjust dietary recommendations accordingly
  - Monitor weight for fluctuation
  - Recommend supplements for patients with nutrient deficiencies (e.g., iron, folate, and calcium)
  - Monitor to be sure the patient receives a GFD during the inpatient stay and assist with completion of dietary menu choices

› **Educate About Diagnosis and Treatment and Promote Parental Emotional Well-Being**
  - Provide detailed education on following a GFD, including
    - eating a GFD high in nutritional value
meal planning
shopping for food
taking supplemental vitamins, iron, and calcium
reading labels on medications, supplements, and foods for information on ingredients and additives, as all can contain gluten

• Provide online sources of information, including CD dietary guides at http://www.celiac.com or https://www.gluten.org
• Assess family anxiety level and coping ability and level of family support for making the prescribed dietary changes; provide emotional support, educate, and encourage discussion on the importance of eating a GFD
• Encourage parent/family visitation, participation in infant care, and rooming-in according to facility protocols
• Request referral, if appropriate, to a
  – social worker for identification of local resources for education and information on a GFD, subsidized sources of gluten-free foods, and support groups
  – mental health clinician for supportive counseling to reduce stress over a diagnosis of CD, if present, and/or the necessity of following a strict GFD
  – child development specialist for supportive counseling to assist with adjustment

Food for Thought

› There is conflicting data on the existence of a “window of tolerance” for gluten introduction and on the protective effect of breast feeding:
  • In a randomized clinical trial, Lionetti et al. (2014) found that rates of celiac autoimmunity and overt CD were higher at 2 years of age in infants who started eating gluten at 6 months compared with infants introduced to gluten at 12 months; however, the difference had disappeared by the time the children were 5 years old
  • In a placebo-controlled randomized clinical trial, Vriezinga et al. (2014) found that daily administration of 100 grams of gluten for 8 weeks to high-risk infants starting at 16 weeks of age did not reduce CD incidence at 3 years of age; breast feeding also made no difference
  • Ivarsson et al. (2013) compared CD incidence in two cohorts of 12-year-olds, one group introduced to gluten at 6 months of age, the other introduced to small amounts of gluten between 4 and 6 months; they reported a significantly lower rate of CD in the early-introduction cohort
  • In an observational study, Størdal et al. (2013) found an association between gluten introduction at 5–6 months of age and slightly lower incidence of overt CD at 2 years compared with introduction at ≤ 4 months or ≥ 7 months; they also noted a higher CD incidence in infants who were breast-fed for ≥ 12 months
  • Myléus et al. (2012) reported a significant association between ≥ 3 parent-reported infections in infants < 6 months of age and higher CD incidence later in life regardless of the type of infection (e.g., common cold, gastroenteritis, otitis media, urinary tract infection). They also noted a synergistic effect between early infectious disease and larger gluten portions

Red Flags

› Serologic tests must be done after 3–6 months of age while the patient is consuming gluten to avoid possible false-negative results

What Do I Need to Tell the Patient/Patient’s Family?

› Emphasize the importance of lifelong adherence to the GFD and continued medical surveillance
  • Many foods are naturally gluten-free, including fruits and vegetables, fresh meats, milk, butter, cheese, eggs, beans, seeds, nuts, corn, and rice
  • Foods to avoid include bread, cereal, oats, and pasta (unless labeled gluten-free) and packaged foods that contain soy and other sauces, marinades, soups, or dressings. It is vital to read product labels
  • Encourage attending a support group for contact with others who face similar health challenges
  • Encourage regular and ongoing appointments with a dietitian to educate and assess dietary adequacy as the child ages
  • Online GFD guidelines and support can be found at the Celiac Disease and Gluten-Free Diet Support Center at www.celiac.com, the American Celiac Disease Alliance at www.americanceliac.org, and the Academy of Nutrition and Dietetics (AND) at www.eatright.org

Related Guidelines

› For guidelines on determining nutrient needs, see Nutritional Assessment and Treatment Goals, above
References


