

**CHRONIC
DISEASES of the
SMALL
INTESTINE**

CELIAC DISEASE

also called gluten-sensitive enteropathy, celiac sprue, nontropical sprue
is an inflammatory condition of small intestine, precipitated by ingestion of grains (wheat, rye, barley) in individuals with certain genetic predisposition.

Etiology

The main serological markers for celiac disease are: antigliadin (AGA), antiendomysial (EMA) and anti-tissue transglutaminase (anti-tTG) antibodies.

Environmental factor: the alcohol-soluble protein fraction of wheat gluten, the gliadins and similar prolamins in rye and barley trigger the intestinal inflammation.

Genetic factor: predisposition to gluten sensitivity is mapped to the HLA-D region on chromosome 6. More than 90% of individuals with celiac disease have DQ2 heterodimer.

Pathogenesis

α_2 – gliadin is a natural digestion product which is important in the pathogenesis of celiac disease. This peptide resists terminal digestion by intestinal brush-border proteases and contains three previously identified antigenic epitops. It also reacts with tissue transglutaminase and stimulates HLA DQ2-restricted intestinal T cells.

Clinical classification of celiac disease

- Classic CD (active form) – characterized by diarrhea and malabsorption syndrome.
- Atypical CD (subclinical, extraintestinal form) – gastroenterological symptoms are absent, extraintestinal symptoms prevail.
- Latent CD – positive serological test but morphological changes are absent.
- Refractory CD – characterized by resistance to treatment.

Clinical features

Celiac disease usually manifests early in life at about 2 years of age after wheat has been introduced into the diet, or later in 20-40 years of life, but can occur at any age.

CD usually has atypical course, without any specific clinical symptoms.

Classic gastrointestinal signs include:

- **Watery diarrhea and weight loss. All major nutrients, most notably carbohydrates, fats, proteins, electrolytes, fat-soluble vitamins, calcium, magnesium, iron, folate and zinc are malabsorbed.**
- **Meteorism, abdominal pain.**
- **Functional dyspepsia, disorders of motor function of gastrointestinal tract, gastroesophageal reflux.**
- **Disorders of exocrine function of pancreas.**

Mechanisms of diarrhea

- Decreased surface area for water and electrolyte absorption
- Osmotic effect of unabsorbed luminal nutrients
- Increased surface area for chloride secretion (crypt hyperplasia)
- Stimulation of intestinal fluid secretion by inflammatory mediators and unabsorbed fatty acids
- Some patients have impaired pancreatic enzyme secretion caused by decreased mucosal cholecystokinin release or bacterial overgrowth that may contribute to diarrhea

Extraintestinal signs of CD

- **Folic acid and/or iron-deficiency anemia, osteoporosis, osteopenia, pathologic fractures and pain in joints**
- **Muscle atrophy, cramps, growth retardation, pallor and dry skin, stomatitis**
- **Peripheral neuropathy, calcification of brain, epilepsy, demyelination damage of central nervous system**
Syndrome of chronic fatigue, neurosis, ataksia
- **Follicular hyperkeratosis and dermatitis herpetiformis (Dühring's disease), psoriasis.**
- **Secondary hyperparathyrosis**
- **Transitory increase of transaminases, hypoalbuminemia, prolongation of prothrombin time**
- **Amenorrhea, infertility, spontaneous abortion, impotence**

Diagnosis

- **Family history of celiac disease, intolerance to grains**
- **Serological assay of antibodies:**
 - **IgA-AGA (antigliadin antibodies)**
 - **IgA-EMA (antiendomysial antibodies)**
 - **IgA-tTG (anti tissue-transglutaminase antibodies)**

Serologic markers are useful in supporting the diagnosis, in screening first-degree relatives and in following the response to gluten-free diet

Diagnosis

Endoscopy of retrobulbar part of duodenum (small intestine) + **BIOPSY** with hystological investigation of mucosa - gold standart for diagnostics of celiac disease.

Characteristic features found on intestinal biopsy include:

- the absence of villi
- crypt hyperplasia
- increased intraepithelial lymphocytes
- infiltration of the lamina propria with plasma cells and lymphocytes.

Additional tests

- Coprological test (steatorrea)
- Liver function test
- Proteinogram
- Glucose level in blood or HbA1
- Electrolytes and microelements contents in blood
- Faeces elastase-1
- Ultrasound of abdomen and thyroid gland
- Colonoscopy or videocapsule endoscopy
- Densitometry for diagnostics of osteoporosis

Diagnostic criteria

The diagnosis of celiac disease is made by characteristic changes found on small intestinal biopsy specimen and **improving** when a gluten-free diet is instituted.

DIFFERENTIAL DIAGNOSIS OF CELIAC DISEASE

- Collagenic sprue
- Tropical sprue
- Lymphoma of the small intestine
- Lactase insufficiency

Complications of celiac disease

- **Ulcerative colitis**
- **T-cell lymphoma of small intestine**
- **Adenocarcinoma of small intestine**
- **Bleeding**
- **Osteoporosis**

Treatment

- LIFELONG GLUTEN-FREE DIET.
- Wheat, rye and barley grains should be excluded from diet
- Rice, corn and oat grains are tolerated (if not contaminated by wheat grain)

Treatment

- **In case of anemia - preparations of iron (tardiferon, tagamet, ferrum-lek, ferrogradumet); folic acid 1 mg/d**
- **in case of the syndrome of malabsorbtion - parenteral nutrition, protein solutions, correction of electrolite balance, Ph balance, enzyme preparations (Creon, Mezym-forte, Pangrol, Festal, Digestal)**

Treatment

- **For prevention and treatment of osteoporosis – preparations of calcium citrate/carbonate (500 mg/d), calcitonin, vitamin D (25000-50000 UI/d)**
- **In severe cases - prednizolon 20-30 mg/d, methylprednizolon 8 mg/d, hydrocortizon 125 mg/d with gradual reduction of the dose.**
- **Follow-up on regular basis, including correction of the diet and treatment, prevention of complications, associated diseases and etc.**

Syndrome of insufficiency of disaccharidases (SID)

- Decreased activity or absence of one or several disaccharidases, which causes disorders in digestion and absorption of disaccharides
- The most typical representative of SID is lactose insufficiency
- SID can be found in 5-15% of white Europeans
- Patients with pathology of small intestine after treatment with antibiotics, contraceptive agents are susceptible to development of SID

ETIOIOLOGY AND PATHOGENESIS

- Disorders of digestion due to insufficiency of enzymes and deficiency of the bile components
- Disorders of digestion due to microbial colonization of the small intestine
- Malabsorption of nutrients due to morphological and functional changes of epithelium of the small intestine
- Affection of specific transport mechanisms (lymphatic and/or circulatory system of the intestine)
- Disorders of the bile acids metabolism due to microbial colonization of the small intestine or impaired intrahepatic circulation of the bile acids
- Disorders of motor function of gastrointestinal system

Main clinical symptoms of SID

- **Spastic pains in abdomen**
- **Diarrea 0,5 - 3 hours after intake of intolerable disaccharide**
- **Polyfecalia**

Syndrome of malabsorption:

- Diarrhea
- Weight loss
- Protein insufficiency and signs of hypovitaminosis which develop due to the processes of the maldigestion and malabsorption in small intestine

CLINICAL symptoms include intestinal and extraintestinal manifestations

- Involvement of the digestive system: diarrhea, steatorrhea, meteorism, abdominal pain, anorexia, nausea.
- Involvement of biliary system: gallstone formation.
- Metabolic disorders: insufficiency of proteins, decrease of energy metabolism, electrolyte disbalance, hypovitaminosis.
- Involvement of the blood system: anemia, hemorrhages.
- Involvement of the bones and muscular system: pain in bones, osteoporosis.
- Involvement of the kidneys: stone formation.
- Involvement of the endocrine system: pituitary insufficiency, hypothyroidism, hypofunction of adrenal cortex and sexual glands.

Physical examination:

- **Weight loss:**

- 1 st. (mild form) - 5 kgs**

- 2 st. (moderate form) - 10 kgs**

- 3 st. (severe form) progressive loss of weight.**

- **Examination:**

- Abdomen – increase in size due to meteorism and formation of gases**

- Palpation - local resistance and hyperesthesia on the left side and around umbilicus**

- Percussion – tympanic sound on small intestine**

DIAGNOSIS OF SID

- ❑ **The clinical signs appear after intake of intolerable disaccharide.**
- ❑ **Coprogram – acid reaction of feces (pH < 6,0)**
- ❑ **Lactose tolerance test - ingestion of 50 g of lactose causes insufficient increase of glucose level in blood; meteorism, tenesmus, diarrhea.**
- ❑ **Morphology - absence of the lactose in biopsy specimen of small intestine**

DIAGNOSTIC CRITERIA :

- **Degree of insufficiency of the feeding :**
 - - mild : albumin (g/l) - 35-30;
transferrin (g/l) - 2,0-1,8;
lymphocytes ($10^9/\mu$) - 1800-1500; skin
reaction on antigens (mm) - 15-10
 - - moderate : albumin (g/l) - 30-25;
transferrin (g/l) - 1,8-1,6;
lymphocytes ($10^9/\mu$) - 1500-900; the
skin reaction on antigens (mm) -10-5
 - severe : albumin (g/l) <25;
transferrin (g/l) <1,6; lymphocytes
($10^9/\mu$) <900; skin reaction on
antigens(mm) - 15-10

Metabolic changes

- Fat metabolism: steatorrhea, hypocholesterolemia, hypoammoniumemia, hypotriglyceridemia
- Carbohydrates metabolism : decrease of glucose level
- Water and electrolyte metabolism : dehydration, hypokaliemia, hypocalciemia

TREATMENT

- ✓ Diet - increased amount of protein (130-135g per day), vitamins, minerals, normal contents of fats and carbohydrates.
- ✓ Elemental therapy – mixtures of balanced chemical composition, containing triglycerides (nutrizan, filotakt)
- ✓ Syntetic therapy - mixtures, consisting of aminoacids, unsaturated fatty acids, polymers of the glucose with low osmolarity.

TREATMENT

- Protein insufficiency – aminoacids solutions, albumin, plasma.
- Electrolite disbalance - saline solutions, glucose, potassium solutions (asparkam, panangin).
- Correction of hypovitaminosis and anemias: iron preparations, vitamin C, vitamins of group B, nicotinic acid.
- Correction of hemostasis - plasma, dicinon, vicasol and others.
- Immunostimulators
- Improvement of digestion and absorbtion processes – enzyme preparations.
- Decrease of meteorism - espumisan.
- Normalization of motor function - spasmolytics and prokinetics.
- Antidiarrhea preparations – imodium, smekta.
- Enterosorbents - enterosgel, smekta .