Celiac Disease

Celiac Disease

- A condition in which there is inflammation of the mucosa of the upper small bowel that improves when gluten is withdrawn from the diet and relapses when gluten is reintroduced
- Up to 1% of the population are affected, though most have clinically silent disease
- Gluten is the entire protein content of the cereals wheat, barley and rye. Prolamins (gliadin from wheat, hordeins from barley, secalins from rye) are damaging factors
- These proteins are resistant to digestion by pepsin because of their high glutamine and proline content and remain in the intestinal lumen triggering immune responses

Inheritance

- There is an increased incidence of celiac disease within families but the exact mode of inheritance is unknown
- 10–15% of first-degree relatives will have the condition, although it may be asymptomatic
- HLA-DQ2 and HLA-DQ8 are associated with celiac disease
- Over 90% of patients will have HLA-DQ2, compared with 20–30% of the general population

Environmental factors

- Breast-feeding and the age of introduction of gluten
- Rotavirus and adenovirus-12

Clinical Features

- Celiac disease can present at any age
- In infancy it sometimes appears after weaning onto gluten-containing foods
- The peak period for diagnosis in adults is in the fifth decade, with a female preponderance
- Many patients are asymptomatic and come to attention because of routine blood tests, e.g. a raised MCV, or iron deficiency
- The symptoms are very variable
- GI symptoms may be absent
- Diarrhea or steatorrhea, abdominal discomfort, bloating or pain and weight loss suggest more severe disease
- Mouth ulcers and angular stomatitis are frequent and can be intermittent
- Infertility and neuropsychiatric symptoms of anxiety and depression occur

- Rare complications include tetany, osteomalacia, or gross malnutrition with peripheral edema may occur
- Neurological symptoms such as parasthesia, ataxia, muscle weakness or a polyneuropathy occur; the prognosis for these symptoms is variable
- There is an increased incidence of atopy and autoimmune disease, including thyroid disease, type 1 diabetes and Sjogren's syndrome
- Other associated diseases include inflammatory bowel disease, primary biliary cirrhosis, chronic liver disease, interstitial lung disease and epilepsy
- IgA deficiency is more common than in the general population
- Long-term problems include osteoporosis which occurs even in patients on long-term gluten-free diets
- Physical signs are usually few and non-specific and are related to anemia and malnutrition

Diagnosis

- Small bowel biopsy is the standard for diagnosis, and is essential because treatment involves a life-long diet that is both expensive and socially limiting
- Endoscopic signs including absence of mucosal folds, mosaic pattern of the surface and scalloping of mucosal folds are often present

Histology

- Histological changes are of variable severity and, though characteristic, are not specific
- Villous atrophy can be caused by many other conditions, but celiac disease is the commonest cause of subtotal villous atrophy
- The villous architecture is almost normal in mild cases, but there are abnormal numbers of intraepithelial lymphocytes
- In severe cases there is an absence of villi, with flattening of the mucosal surface
- Histological examination shows crypt hyperplasia with chronic inflammatory cells in the lamina propria
- The most severe histological change with mucosal atrophy and hypoplasia is seen in patients who do not respond to a gluten-free diet

Serology

- Persistent diarrhea, folate or iron deficiency, a family history of celiac disease and associated autoimmune disease are indications for serological testing
- The most sensitive tests are for anti-endomysial and anti-tissue transglutaminase antibodies
- The sensitivity of these tests is > 90% though both are not always positive in the same subject
- Titers of either correlate with the severity of mucosal damage so they can be used for dietary monitoring

HLA typing

- HLA-DQ2 is present in 90–95% of celiac disease patients and HLA-DQ8 in about 8%
- The absence of both alleles has a high negative predictive value for celiac disease
- HLA typing is useful for ruling out the disease, for example in patients already on a gluten free diet

Further Investigation

- Mild to moderate anemia is present in 50% of cases. Folate deficiency is common, often causing macrocytosis. B12 deficiency is rare. Iron deficiency due to malabsorption of iron and increased loss of desquamated cells is common
- A blood film may therefore show microcytes and macrocytes as well as hypersegmented polymorphonuclear leucocytes
- In severe cases, biochemical evidence of osteomalacia may be seen (low calcium and high phosphate) and hypoalbuminemia
- Bone densitometry (DXA) should be performed on all patients because of the risk of osteoporosis

Management

- Replacement of minerals and vitamins, e.g. iron, folic acid, calcium, vitamin D, may be needed initially to replace body stores
- Treatment is with a gluten-free diet for life. Dietary elimination of wheat, barley and rye usually produces clinical improvement within days or weeks
- Morphological improvement often takes months, especially in adults
- Oats are tolerated by most celiac patients, but must not be contaminated with flour during their production
- Meat, dairy products, fruits and vegetables are naturally gluten free and are all safe
- Many patients do not keep to a strict diet but maintain good health
- The long-term effects of this low gluten intake are uncertain but osteoporosis can occur even in treated cases
- The usual cause for failure to respond to the diet is poor compliance
- Dietary adherence can be monitored by serial tests for endomysial antibody (EMA) and tissue transglutaminase
- If clinical progress is suboptimal then a repeat intestinal biopsy should be taken
- If the diagnosis is equivocal a gluten challenge, i.e. reintroduction of gluten with evidence of jejunal morphological change, confirms the diagnosis

Complications

- A few patients do not improve on a strict diet and are said to have unresponsive celiac disease
- Often no cause is found, but enteropathy-associated T cell lymphoma (EATCL), ulcerative jejunitis or carcinoma are sometimes responsible
- The incidence of EATCL and small bowel adenocarcinoma is increased in celiac disease
- Ulcerative jejunitis presents with fever, abdominal pain, perforation and bleeding
- Diagnosis for these conditions is with barium studies but laparotomy with full-thickness biopsies is often required. Steroids and immunosuppressive agents, e.g. azathioprine, are used
- Carcinoma of the esophagus as well as extra-gastrointestinal cancers are also increased in incidence. Malignancy seems to be unrelated to the duration of the disease but the incidence is reduced by a gluten-free diet

Thank You