INTRODUCTION

Iron malabsorption is an important cause of iron-deficiency anaemia (IDA). Coeliac disease-induced malabsorption in the small intestine also causes IDA. Furthermore, severe IDA may be the only sign of coeliac disease without any gastrointestinal symptoms. Eighty-five percent of patients with IDA recover from anaemia after iron-replacement therapy (1-3).

In 15-30% of patients with IDA, the underlying pathology is not known. We present here two cases of coeliac disease who had a 3-year history of unexplained severe iron-deficiency anaemia.
Case 1. A 41-year-old female with complaints of weakness, pallor, and palpitation was admitted to the internal medicine clinic of Turgut Ozal Medical Center, Malatya, for 3 years of regular oral iron treatment of refractory anaemia. Physical examination revealed pallor and systolic murmur on the cardiac apex. A complete blood count showed: haemoglobin of 4.6 g/dl, white blood cell count of 5.500/mm³, platelet count of 367,000/mm³, mean corpuscular volume of 56 fl, and mean corpuscular haemoglobin of 16 pg. Serum iron was 22 µg/dl, serum transferrin 508 mg/dl, and ferritin 11 ng/dl. A blood-smear examination revealed hypochromia, anisocytosis, poikilocytosis, and microcytosis. Anti-gliadin IgA antibody was 18.25 U (normal value: 0-10 U) and anti-gliadin IgG antibody was 31.0 U (normal value: 0-24 U).

Case 2. A 34-year-old female with complaints of weakness for 3 and a half years was admitted to the clinic with refractory anaemia to oral iron treatment. She was regularly taking iron-containing drugs for the last 3 and a half years. She was pale, and had finger clubbing. Physical examination was otherwise normal. A complete blood count showed: haemoglobin of 5.2 g/dl, white blood cell count of 6,700/mm³, platelet count of 287,000/mm³, mean corpuscular volume of 62 fl, and mean corpuscular haemoglobin of 17 pg. Serum iron was 16 µg/dl, serum transferrin 520 mg/dl, and ferritin 9 ng/dl. A blood-smear examination revealed hypochromia, anisocytosis, poikilocytosis, and microcytosis. Antigliadin IgA antibody was 21.10 U, and anti-gliadin IgG antibody was 29.5 U.

Both the patients had no symptoms of malabsorption, such as diarrhoea, abdominal pain, and steatorrhea, but both had normal menstruation. They also did not have a history of operation on gastrointestinal, gynaecologic or pulmonary system. Biochemical tests, including serum potassium, sodium, calcium, phosphorus, creatinine, alkaline phosphatase, cholesterol, partial thromboplastin time, immunoglobulin A, G, M, tumor markers, folic acid, vitamin B12, haptoglobin, acid haemolysis test (Ham’s test), and thyroid function tests, were within normal limits. Serum protein level and protein electrophoresis were also normal. The erythrocyte sedimentation rates were 12 and 15 mm/h respectively. No parasite was detected in faeces; the test was repeated 3 times in both the patients, and the lipid tests of faeces were negative in both the patients. An endoscopical examination of the stomach, small bowel, and large bowel revealed no focus of bleeding, but there were subtotal atrophy in the duodenal mucosas and flattening and loss of villi in the biopsy specimens. Only gluten-free diet with no iron supplementation was given as treatment, and no antibiotic was used. An examination of both the patients after 7 months showed an improvement in the haemoglobin levels (12.2 and 13.1 g/dl respectively), and endoscopical and pathological examinations of the small intestine were found to be normal.
Coeliac disease (gluten-induced enteropathy) is a chronic, probably hereditary, illness of unknown aetiology, occurring in both children and adults, and is manifested clinically by steatorrhoea and deficiencies produced by intestinal malabsorption. The metabolites of gluten are thought to trigger an immunological reaction that leads to the damage of enterocytes and finally to malabsorption (4). The symptoms and signs of coeliac disease may first appear in infancy, disappear in late childhood, and may reappear in the third to sixth decade. The proximal small intestinal mucosa is the area mostly affected by the disease.

Diagnosis is verified by the finding of a flattened mucosa on jejunal biopsy and by the subsequent clinical and histological improvement on a gluten-free diet. The positivity of serum anti-gliadin antibody IgA is also important. Response to gluten-free diet may even be seen in a few days, but in some cases it may be seen even months later. After gluten-free diet, histopathological examinations of the small intestine should be improved to reach definitive diagnosis of coeliac disease (2).

In 15-30% of patients with IDA, its cause may not be identified (1-3). Blood loss and low-iron-containing diet are the two reasons that are mostly encountered in the aetiology of IDA (3). IDA, caused by decreased intake of iron, is a problem in developing countries, and malabsorption is also an important cause of IDA.

Symptoms of IDA may be the only complaint of a patient with coeliac disease on admission. These symptoms may appear prior to symptoms related with the gastrointestinal system (5,6). In 1994, of 170 patients with IDA who had no coeliac disease-related symptoms, Gordan et al. (7) diagnosed 5 (3%) coeliac disease cases. Hin et al. recently reported that 50% of patients suffering from coeliac disease may present with IDA without any gastrointestinal symptoms in a primary-care setting (8). The prevalence of subclinical/silent forms of coeliac disease has been increasing, which may be due to greater diagnostic awareness and better application of screening. IDA is also the most frequently-observed extraintestinal symptom (9).

When evaluating IDA, small intestinal biopsy is not a routine application to rule out coeliac disease (10,11). However, the presence of mosaic pattern mucosa with scalloping of duodenal folds, reduction of number of folds, and occasionally nodular mucosa in histologically-confirmed coeliac disease patients has recently been reported; all of these signs have been observed in the second part of the duodenum. These endoscopic markers had a sensitivity of 87.5% and specificity of 100% (12). Ackerman et al. (13) examined biopsy specimens in 93 patients with IDA, in 23 patients with steatorrhoea, and in 37 patients with idiopathic diarrhoea histopathologically. In the IDA group, 11 patients were diagnosed as coeliac disease, whereas only 2 patients in the steatorrhoea group were found to have coeliac disease.

Achylorhydria, postgastrectomy syndrome, atrophic gastritis, intestinal motility disorders, short bowel syndrome, shortening of the intestinal passage time, gastrojejunostomy, and functional degenerations in the proximal small intestinal segments are the causes of iron malabsorption in the small intestine. In our cases, examinations of the small intestine yielded the diagnosis of coeliac disease. There was villous atrophy in the duodenal biopsy specimens. In the differential diagnosis, tropical and non-tropical sprue, giardiasis, intestinal lymphoma, and hypogammaglobulinaemia should be investigated. Although rarely, acute and chronic infectious enteritis, eosinophilic enteritis, colagenous sprue, cow milk protein intolerance, immunodeficiency syndromes, and gastrinoma will mimic the histological findings of coeliac disease.

Possible reasons of IDA in coeliac disease include: (a) the defect and decrease in the absorptive surface area, (b) decreased iron intake due to vomiting and loss of appetite, and (c) promotion of iron loss due to intestinal blood loss and degeneration of enterocytes.

In different clinical studies, microcytic or macrocytic anaemias were reported in 10-80% of patients with coeliac disease (14-21). In the paediatric group, 30% of patients with coeliac disease were found to have IDA (19), whereas in the adult group of coeliac disease, macrocytic
anaemia due to folic acid deficiency was found in 30% of patients (18). Especially in adult female patients with normal menstrual blood loss, coeliac disease should be born in mind in iron-deficiency anaemia resistant to chronic oral supplementation, even if there are no gastrointestinal signs and symptoms reminding coeliac disease.
REFERENCES


