Celiac Disease in Childhood: Evaluation of 140 Patients

Çocukluk Çağında Çölyak Hastalığı: 140 Hastanın Değerlendirilmesi

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Abstract

Objective: Celiac disease (CD) is a lifelong gluten-sensitive intestinal enteropathy that is multifactorial in its etiology. In the present study, we evaluated basic anthropometric, clinical, laboratory, and histological features of 140 Turkish children with CD. We particularly underscored the association of CD with other autoimmune diseases.

Materials and Methods: During the period from 1999 to 2005, CD was diagnosed in 140 children according to ESPGAN criteria. The age, gender, clinical findings, hematological, and biochemical parameters at diagnosis were noted. Symptoms and signs were recorded. Endoscopic intestinal biopsies were taken from all children.

Results: Of the 140 children with CD, 75 (53.6%) were female, and 65 (46.4%) were male. Mean age was 8.56 ± 4.43 years (range 13 months to 18 years). The most frequent symptom was failure to thrive (81.4%), followed by chronic diarrhea (60%). Of the children with CD, nine (6.4%) had type 1 diabetes mellitus (DM), six (4.3%) had familial Mediterranean fever, three (2.1%) had alopecia areata, three (2.1%) had vitiligo, three (2.1%) had Down syndrome, two (1.4%) had lung tuberculosis, two (1.4%) had autoimmune hepatitis, two (1.4%) had growth hormone deficiency, one (0.7%) had osteogenesis imperfecta, and one (0.7%) had Floating Harbor Syndrome. Elevated serum levels of ALT, CK and AST were detected in 48 (34.8%), 50 (38.2%), and 67 (48.6%) children, respectively.

Conclusion: The spectrum of clinical findings is very wide. In order to avoid overlooking CD in patients with extra intestinal symptoms and signs, physicians, especially pediatricians, should be informed about new atypical manifestations of CD.

Keywords: Celiac disease, Clinical findings, Child

Özet

Amaç: Çölyak Hastalığı (ÇH) multifaktöryel etyolojisi hayat boyu davam eden glutene duyarlı incebarsak hastalığıdır. Bu çalışmada ÇH liken 140 Türk çocuğunun histolojik, laboratuvar, klinik, antropometrik bulguları değerlendirildi.


Bulgular: ÇH liken 140 çocuğun 75 (%53,6’ı) kız, 65 (%46,4’ü) erkek idi. Olguların ortalama yaşları 8,56 ± 4,43 yıl (13 ay-18 yaş). En sık görülen semptom büyüme gelişme gerilisi idi. ÇH’ liken 9 (%6,4’ü) tıba tip 1 diabetes mellitus (DM), 6 (%4,3’) sında ailevi akdeniz ateş, 3 (%2,1’) sında alopesia areata, 3 (%2,1’) sırında vitiligo, 3 (%2,1’) sırında Down sendromu, 2 (%1,4’) sırında akciğer tüberkülozu, 2 (%1,4’) sırında autoimmune hepatitis, 2 (%1,4’) sırında büyüme hormonu eksikliği, birinde (%0,7) osteogenesis imperfekta, birinde (%0,7) Floating Harbor sendromu saptandı. ALT, AST ve CK’nın serum düzeylerinde artış sırası ile şıngle id: 48 (%34,8), 50 (%38,2), and 67 (%48,6).

Sonuç: ÇH liken çocuklarda klinik bulguların dağılımı çok geniş idi. Ekstra intestinal semptomlu hastalarda ÇH tanısı göze çarparak mak için hekimler, özellikle çocuk hekimleri ÇH’nin yeni atipik bulguları hakkında duzenli olarak bilgilendirilmelidirler.
Introduction

Celiac disease (CD) is a lifelong gluten-sensitive intestinal enteropathy that is multifactorial in its etiology. The disease provides an exciting model where both genetic and environmental factors play an important role [1,2]. Epidemiological knowledge of CD has seen several changes during the last decade of the 20th century. Prior to the 20th century, celiac disease was considered relatively rare in most European countries [3,4]. However, several recent European studies have shown a population based screening prevalence for the disease of 1:150 to 1:300 [5]. Indeed, in the first CD prevalence study in Turkey, we found that CD was highly prevalent, with a rate of 1:115 among healthy school-age children [6].

Typical disease symptoms include chronic diarrhea, fatigue, and failure to thrive. These symptoms are associated with lesions in the upper small intestine that are characterized by villous atrophy, crypt cell hyperplasia, and infiltration of the lamina propria and epithelium with lymphocytes, macrophages, and plasma cells [2]. Atypical celiac disease, i.e., celiac disease that presents with extra-intestinal manifestations in the absence of diarrhea, is well recognized worldwide [7].

In the present study, we evaluated basic anthropometric, clinical, laboratory, and histological features of 140 Turkish children with CD. We particularly underscored the association of CD with other autoimmune diseases.

Materials and Methods

Between 1999 and 2005, 140 children with CD were diagnosed according to ESPGAN criteria in this retrospective study [8]. None of these patients showed cardiac, renal, or allergic abnormalities that would interfere with growth. The age, gender, clinical findings, hematological, and biochemical parameters at diagnosis were noted. Symptoms and signs were recorded. Endoscopic intestinal biopsies were taken from all children, and histopathological findings were evaluated. The degree of villous atrophy was graded according to the modified Marsh criteria as follows: 0-mucosa with normal villous architecture; I-mucosa with normal villous architecture and more than 30% increase in IEL, and crypt hyperplasia (IEL)/100 enterocytes; II-mucosa with normal villous architecture and greater than 30% increase in IEL, and crypt hyperplasia; and III-mild (IIIA), subtotal (IIIB), and total (IIIC) villous atrophy. Data analysis was performed using SPSS 10.0 program. Mean ± standard deviation (SD), chi-square, and Mann Whitney-U tests were used for statistical analysis. Correlation coefficients were calculated by Pearson's method. All p-values ≤ 0.05 were considered statistically significant.

Results

Of the 140 children with CD, 75 (53.6%) were female, and 65 (46.4%) were male. Mean age was 8.56 ± 4.43 years (13 months to 18 years) at diagnosis. A total of 19 patients (13.6%) were younger than two years of age.

The most frequent symptom was failure to thrive (81.4%), followed by chronic diarrhea (60%). The other symptoms were weight loss (58.5%), abdominal pain (55%), vomiting (51.4%), anorexia (32.9%), and inability to walk (3.6%). Short stature as the sole primary symptom was seen in only 24 (17.1%) patients. Clinical and laboratory findings of patients are shown in Table 1 and 2. Of 140 patients with CD, 85 (60.7%) had the classical form, while the remaining 55 (39.3%) had an atypical form.

Of the 140 patients, 15 (10.7%) were identified as having CD via a screening process. Of all children with CD, nine (6.4%) had type 1 diabetes mellitus (DM), six (4.3%) had familial Mediterranean fever, three (2.1%) had alopecia areata, three (2.1%) had vitiligo, three (2.1%) had Down syndrome, two (1.4%) had lung tuberculosis, two (1.4%) had autoimmune hepatitis, two (1.4%) had growth hormone deficiency, one (0.7%) had osteogenesis imperfecta, and one (0.7%) had Floating Harbor Syndrome.

IgA-antigliadin antibody (136), IgG- anti-gliadin antibody (138), and EmA (130) were found to be positive in 80.8%, 81.2%, and 90% of the patients, respectively. Selective Ig A deficiency was found in 6.3%. Elevated serum levels of alanine aminotransferase (ALT), creatine phosphokinase (CK) and aspartate aminotransferase (AST) were detected in 48 (34.8%), 50 (38.2%), and 67 (48.6%) patients, respectively (Table 1). Five (3.6%) of our patients were admitted with clinical rhabdomyolysis.

Iron deficiency anemia was detected in 64 (45.7%) patients, and megaloblastic anemia with low serum vitamin B12 or folate acid levels was detected in 15 children (10.7%). Mean values of some laboratory findings of patients with CD are shown in Table 2.

Discussion

Celiac disease is an autoimmune disorder triggered by the cereal protein gluten. The clinical manifestations of CD vary with the age of the patient, the duration and extent of disease, and the presence of extra intestinal complications [8,9]. We evaluated the clinical and laboratory features of 140 children with CD. Although a broad spectrum of clinical presentations was noted, classical CD was more common than the atypical form. However, given the increasing awareness of the extra-intestinal manifestations of CD and the increasing tendency to screen for the disease...
Conflict interest statement
The authors declare that they have no conflict of interest to the publication of this article.

32% of pediatric patients with CD, and five of them (4.3%) were diagnosed with CD due to EST. In our study, elevated serum levels of ALT, CK, and AST were detected in 48 (34.8%), 50 (38.2%), and 67 (48.6%) patients, respectively. None of our patients were diagnosed as CD due to EST.

It is known that gluten hepatitis, a benign condition characterized by a mild elevation in serum aminotransferase levels in the setting of modest lobular and portal tract inflammation, is responsive to a gluten-free diet; indeed, such a diet results in complete remission and normalization of the biochemical and histological signs of hepatitis [15,20]. The pathogenesis of the liver damage is poorly understood.

No published studies including either adults or children with CD show data on serum CK levels. Elevated serum levels of CK were detected in 50 (38.2%) patients in our study. Because five (3.6%) of our patients were admitted with clinical rhabdomyolysis, we attributed high CK levels of children with CD to probable muscle involvement in CD.

Anemia is a frequent problem in cases with CD regardless of whether the anemia is the index presenting symptom or not, thus, all CD cases need to be evaluated for iron-deficiency anemia [23,24]. Doganci et al. reported that more than 50% of all cases had iron-deficiency anemia [24]. We detected iron-deficiency anemia in 45.7% of our patients.

Oral mucosal lesions, alopecia areata, and vitiligo occur more frequently in patients with dermatitis herpetiformis than in the general population [25]. No study showing the relationship between these mentioned skin disorders and CD has been performed in Turkey; however, CD prevalence among patients with alopecia was reported to be 1:116 and 1:89 in two different studies performed in Italy [26,27]. No relationship between vitiligo and CD was noted [28]. Among our patients, three (2.1%) had alopecia areata, and three (2.1%) had vitiligo.

In conclusion, CD is as common a disease in children as in adults. The spectrum of clinical findings is very wide and tends to manifest with extra intestinal forms. For that reason, in order to avoid overlooking CD in patients with extra intestinal symptoms and signs, physicians, especially pediatricians, should be informed about new atypical manifestations of CD.

**Conflict interest statement** The authors declare that they have no conflict of interest to the publication of this article.

**References**