Geliş Tarihi / *Received*: 01.07.2010 • Kabul Tarihi / *Accepted*: 09.12.2010

THE EVALUATION OF SHORT STATURE AND BONE AGE IN CHILDREN WITH CELIAC DISEASE

ÇÖLYAK HASTALIĞI OLAN ÇOCUKLARDA BOY KISALIĞI VE KEMİK YAŞININ DEĞERLENDİRİLMESİ

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ABSTRACT

Untreated Celiac Disease (CD) may lead to short stature, decreased growth velocity and delayed skeletal development. However the role of delayed skeletal development on catch up growth in children with CD receiving gluten free diet (GFD) is not well established. We aimed to evaluate the effect of delayed skeletal development and duration of gluten free diet on growth in celiac patients with short stature in this study. Twenty patients with CD and short stature (height SDS <-1.5 SDS) were analyzed retrospectively. Chronogical age, bone age, height standart deviation score (HSDS), pubertal stage and growth velocity at the diagnosis and during the folllow- up were recorded. Bone age delay (BAD) was 2.8 ±1.8 years at the diagnosis. HSDS was statistically higher in cases whose bone age delay were less than 2 years. It was found that there was no significant difference in growth velocity in the first 2 years of GFD between the children with BAD more than 2 years and less than 2 years. We showed that growth velocity didn't differ at the end of the first and second year of GFD. Also we concluded that, bone age delay doesn't seem to be a promising criteria for evaluating catch up growth in CD

Key words: Bone age, celiac disease, short stature

Abbreviations:

CD: celiac disease, GFD: Gluten free diet, BA: bone age, BAD: bone age delay, HSDS: height standart deviation score, GVDSDS: growth velocity standart deviation score, n:number

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ÖZET

Tedavi edilmemiş Çölyak Hastalığı boy kısalığı, büyüme hızında azalma ve iskelet gelişiminde gecikmeye yol açabilir. Glutensiz diet alan Çölyak hastalıklı çocuklarda büyümeyi yakalamada gecikmiş iskelet gelişiminin rolü tam olarak bilinmemektedir. Biz bu çalışmada kısa boylu Çölyak hastalarında gecikmiş iskelet gelişimi ve glutensiz diet süresinin büyümeye etkisini değerlendirmeyi amaçladık. Çölyak hastası ve boy kısalığı olan yirmi hasta (boy SDS<-1.5 SDS) retrospektif olarak analiz edildi. Başlangıçtaki ve izlem sürecindeki kronolojik yaşları, kemik yaşları, boy standart deviasyon skorları, pubertal evreleri ve büyüme hızları kayıt edildi. Başlangıçtaki kemik yaşı geriliği 2.8 ± 1.8 yıldı. Kemik yaşı geriliği 2 yıldan az olan olgularda boy standart deviasyon skorları istatiksel olarak anlamlı yüksekti. Glutensiz dietin ilk 2 yılında kemik yaşı geriliği iki yıldan fazla ve iki yıldan az olan olgular arasında büyüme hızında anlamlı farklılık saptanmadı. Biz, glutensiz dietin 1. ve 2. yılları sonunda büyüme hızları arasında farklılık olmadığını gösterdik. Ayrıca Çölyak hastalığında kemik yaşı geriliğinin büyümeyi yakalamayı değerlendirmede umut verici bir kriter olarak görünmediği sonucuna vardık.

Anahtar Sözcükler: Kemik yaşı, çölyak hastalığı, kısa boy

INTRODUCTION

Celiac disease is a chronic malabsorptive disorder induced by exposure to gluten. It is clearly showed that short stature is one of the most well- known extra intestinal manifestations of celiac disease (1-4). This immunmediated chronic enteropathic condition is the most common organic cause of impaired linear growth and it's more frequent than growth hormone deficiency (4-6). Delayed bone age, normal levels of serum IGF 1, normal growth hormone response to stimulatory tests and decreased IGF binding protein 3 are characteristics of the endocrinological pattern of short stature due to CD (7). In CD patients, growth hormone deficiency may also be observed but growth hormone secretion usuallly normalizes during the GFD and a growth spure occurs. GFD usually leads to complete catch- up growth within 2-3 years (8).

There are limited data about the role of bone age delay at diagnosis on catch-up growth with GFD in CD cases with short stature.The aim of this study is to evaluate the relationship between bone age delay, GFD duration and catch-up growth in CD.

MATERIALS - METHODS

The children with short stature (without any other symptoms) referred to our pediatric endocrinology and gastroenterology clinics whose HSDS were below -1.5 SDS for appropriate age and sex were studied retrospectively. Their medical charts were rewieved and data including their demographic characteristics , anthropometric measurements were recorded. All cases were screened for CD by antigliadin and antiendomysial antibodies (AGA IgA, AGA IgG, EMA). Serum IgA concentrations were measured in order to exclude false negative results.

Serum IgA level was within normal range in all cases. Cases with positive sera underwent endoscopic examination of the upper gastrointestinal tract with at least four biopsies of the distal duodenal mucousa. The diagnosis of CD was established on the basis of the criteria supported by European Society of Pediatric Gastroenterology, Hepatology and Nutrition (EPSGHAN) (9) . 32 children were diagnosed with CD and they started to recieve GFD. Children who have coexisting genetic, metabolic or endocrinologic problems such as Turner syndrome (n: 2), Down syndrome (n:1) , empty cella (n: 1), occult pseudohypoparathyrodism (n: 2) were excluded. 4 patients whose follow up period were less than 1 year and 2 patients who didn't keep to GFD were also excluded. Thus, 20 patients (11 girls, 9 boys) with short stature and CD were included into the study.

At the baseline physical examination , pubertal staging (PS) according to Tanner Stages and bone age (BA) were noted for all patients. Bone age was determined on the basis of X-ray of the left hand according to the method Greulich and Pyle. HSDS and growth velocity standart scores (GVSDS) calculated on the basis of national standarts for each patient were also noted. The standart deviation score was calculated according to the formula: (Patient height- 50th percentile height appropriate for patient age)/ Standart deviation. BAD was defined as the difference between bone age and chronological age. These parameters were re-evaluated anually during the follow up period. HSDS differences after the first and second year of the GFD (ΔHSDS1, ΔHSDS2) were also recorded. ΔHSDS1 was calculated according to the formula: HSDS at the end of the first year- HSDS at the beginning. ΔHSDS 2 was also calculated according to the formula: HSDS at the end of the second year- HSDS at the beginning. All cases were subdivided according to duration of GFD (maximum 2 years/more than 2 years) , BAD (maximum 2 years/ more than 2 years), GVSDS (less than -1 SDS/ minimum -1 SDS)

Data were reported as means and standart deviation (± SD) . Changes in all parameters were analyzed using Wilcoxon signed test and p value <0.05 was considered significant.

RESULTS:

11 of 20 patients were female and 9 were male. The mean age of all cases was 11.7± 2.9 years. Bone age delay (BAD) was 2.8 ±1.8 years at the diagnosis.The clinical features of the children is shown in Table 1.

Table 1: Characteristics of the patients with CD.

	n=20
CA (year)	11.7 ± 2.9 (3.5- 15.9)
BA (year)	9.1± 2.7 (3-13)
BAD (year)	2.8 ±1.8 (0-5.5)
Puberty	13 prepubertal/ 7 pubertal
HSDS	-2.9±0.9 [(-5.3)- (-1.9)]
GFD duration (year)	2.8±1.1 (1.8- 4.4)
ΔHSDS	1.3±1.2 [(-0.6)- (3.5)]

HSDS was higher in the group whose BAD were less than 2 years. However ΔHSDS didn't change significantly in the first 2 years period of GFD on follow up. Table 2 shows comparison of all patients according to BAD.

Table 2: Characteristics of patients according to BAD at the diagnosis

	BAD≤2 year (n=8)	BAD>2 year (n=12)	P
CA (year)	11±3.4	12.3±2.7	0.001 *
BA (year)	10.1±3.3	8.4±2.2	0.001 *
HSDS	-2.9±0.6	-3±1	0.001 *
GFD duration (year)	3.1±1.3	2.5±1	0.001 *
ΔHSDS1	0.8±0.7	0.8±1	NS
ΔHSDS2	1.3±1.2	1.1±1	NS
Puberty (prepubertal/pubertal)	5/3	7/5	

NS: Non significant

We showed that the duration of GFD hasn't got an effect on growth velocity. The GVSDS values were approximately similar on the first and second year of GFD (Table 3).

Table 3: Growth velocity (GVSDS) of cases at the end of the the first (GFD1) and the second (GFD2) year of GFD.

	Number of cases on GFD1	Number of cases on GFD 2
GVSDS< -1 SD	4	3
GVSDS≥ -1 SD	16	17

As a result, we found that bone age delay at the diagnosis doesn't influence catch-up growth of children with CD recieving GFD. Also we showed that growth velocity isn't related to the duration of GFD.

DISCUSSION

It is emphasized that there are considerable changes in the clinical presentation of CD; asymptomatic patients diagnosed by screening are increasing significantly (10). However, CD still remains an important disorder that must be excluded in the diagnostic approach to short stature(11,12). Kuloğlu et al. reported that short stature is one of the most common extra intestinal findings (%31.2) of CD in Turkish children (13). The pathogenesis of CD- associated short stature is controversial. Although, it is known that growth hormone deficiency or growth hormone resistance may lead to short stature and poor catch- up growth in CD (14-16). It's also reported that anti- pituitary antibodies leading to otoimmun hyphophysitis may contribute to growth impairment/ poor clinical response in CD (17,18).

Catch-up growth is defined as supranormal height velocity. After the beginning of the GFD, there's a rapid recovery of the somatotrophic axis and catch- up growth usually occurs (19). Here, we studied the effect of BAD on growth velocity in CD. All of the patients had BAD and the patients with BAD more than 2 years were significantly shorter than the others. BAD has an accordance with short statuture, therefore we emphasize that it's essential to evaluate for CD in children with short stature and BAD. Salardi et al reported that bone age delay at the diagnosis is a positive predictor of catch- up growth in CD (20). However we didn't find a relationship between BAD and catch-up growth in our study. ΔHSDS 1 and ΔHSDS2 were similar in two groups. Giovenale et al recommended that GH secretion must be evaluated in cases with CD showing no catch- up growth after an appropriate period of GFD (21). On follow up, catch- up growth occured in our patients and we didn't screen for growth hormon deficiency.

We also evaluated the effect of GFD period on catch-up growth in CD. GVSDS didn't differ at the end of the first and second year of GFD. Patwari et al. (22) reported that GFD leads to normalization of body mass and an improvement in growth in the first 4 years period of GFD. Further studies are needed for evaluating the relationship between GFD period and catch- up growth in CD.

In conclusion, although it's small in size, this study indicates that short stature children with CD generally have BAD more than 2 years. We report that BAD at the diagnosis doesn't seem to be a promising criteria for evaluating catch up growth in CD. Gluten free diet is associated with rapid catch- up growth in CD.

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