Chromosomal Abnormalities in 344 Patients who Were Referred to Cytogenetics Laboratory with Pre-Diagnosis of Short Stature, Turner Syndrome and Sex Developmental Disorders

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If the height is more than 2 standard deviations below the mean for age and gender, it is defined as a short stature. Genetic factors are the most important factors playing role in short stature. Turner syndrome is a disorder caused by the absence of all or part of one of the X chromosomes or its structural abnormalities and is characterized by short stature, webbed neck, growth retardation, lymphedema of the hands and feet, low nuchal hairline, infertility, and widely spaced nipples. The situation where gonads, internal and/or external genitalia are inappropriate is known as ambiguous genitalia or disorders of sex development (DSD). In this study, cytogenetic test results of 344 patients with preliminary diagnosis of short stature or Turner syndrome or DSD were retrospectively evaluated. Cytogenetic analysis was performed in the genetics laboratory of Pediatrics Department, Faculty of Medicine, Ege University between the period of January 2010 and January 2015. The chromosomal abnormality was observed in 10 (49%), 31 (13.13%), and 9 (22.5%) cases of 68, 236, and 40 pediatric patients with short stature, Turner syndrome, and DSD indications, respectively. Based on the results of this study, structural chromosomal abnormalities constituted 80% of the genetic factors that caused short stature and the numerical chromosomal abnormalities constituted 80.65% of the genetic disorders that led to Turner syndrome. The 77.8% of patients with DSD or ambiguous genitalia had 46,XY karyotype and structural abnormalities were observed in the rest (22%). Because of high rate of chromosomal abnormalities, cytogenetic tests should always be performed in patients with the diagnosis of short stature, Turner Syndrome, and DSD.

Key words: Short stature, Turner syndrome, disorders of sex development, chromosomal abnormality, cytogenetic analysis

Genotype-Phenotype Correlation and Follow-Up Features in Cases with Congenital Hyperinsulinism (CHI)

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Introduction: There is a genotype-phenotype correlation in cases with congenital hyperinsulinism (CHI). Genetic analysis that will be held in early stages is important for the treatment choice and follow-up of the patient. There have been 9 gene mutations defined in the genetic diagnosis of CHI. These are: K-ATP channel genes (*ABCC8, KCNJ11*), G*LUD1, HADH, GCK, HNF4A, UCP2, SLC16A*1 gene mutations.

Methods: The follow-up data and the phenotypic and genotypic features of the 7 patients who were diagnosed with CHI between the years 2009 and 2014 were evaluated.

Results: All our patients were diagnosed with hyperinsulinemic hypoglycemia in the first 48 hours. There was consanguinity between the parents of 4 patients (57%). Hyperinsulinism was temporary in 5 and permanent in 2 patients. Six cases were responsive to the diazoxide treatment, while one case was unresponsive and near total pancreatectomy was performed in the second month of its life. Motor-mental retardation and epilepsy occurred due to recurrent hypoglycemia and the patient developed post-op portal venous thrombosis. Mutations of the known genes were found in 3 of the patients (42.8%). A homozygote p.R1419C mutation in the *ABCC8* gene of one diazoxide-responsive case with permanent CHI was detected. A diazoxide-responsive case with a heterozygous p.R365C mutation in the *KCNJ11* gene and a case with a heterozygous p.R1539Q mutation in the *ABCC8* gene showed remission in the 18th day and the 6th month respectively and the drugs were discontinued. The features of the cases are presented in the table.

Conclusion: Genetic causes were detected in approximately 40% of our patients which is consistent with the literature. Other genes could play a role in cases without mutations.

Key words: Congenital hyperinsulinism, genotype-phenotype correlation