Etiologic Classification of 46, XX Disorders of Sexual Differentiation According to Chicago Consensus: Single Center Results

Ayla GÜVEN[1,2], Metin YILDIZ[2]
Saglik Bilimleri University, Zeynep Kamil Women and Children Hospital, Pediatric Endocrinology Clinic[1], Göztepe Education and Research Hospital, Pediatric Endocrinology Clinic[2], Istanbul, TÜRKİYE

Introduction

Objective: The aim of the study was to describe the etiologic diagnosis, clinical characteristics in children with 46,XX disorder of sexual development (DSD).

Methods

The 85 patients who have 46,XX karyotype, were enrolled to the retrospective study. The definitive diagnosis was made by presentations and clinical findings, gonadal morphology and genital anatomy of patients, basal and stimulated hormone results, imaging methods, molecular genetic analyzes and feminizing or masculinizing genitoplasty. All data obtain from hospital records.

Results

Types and ratios of each presentation of the 86 patients with 46,XX DSD were as follows.:

Majority of the patients were in androgen excess group (n:60, 69.7%).

Patients with disorders of ovarian development were the second (n:21, 24.7%).

Among the androgen excess group, salt-wasting congenital adrenal hyperplasia (SW-CAH) was the major group (55%), simple virilization-CAH (SV-CAH) was the second (40%).

Parental consanguinity detected in %63.3 in SW-CAH and %54.5 in SV-CAH. Siblings of seven patients with SW-CAH and siblings of four patients with SV-CAH have same disease.

CYP21A2 mutations were detected in 26 patients with CAH. Two patients had *CYP11B1* mutation. One patient had *CYP19A1* mutation. Etiology was not found in two patients with clitoromegaly.

Feminizing genitoplasty was performed in four of six patients who were given male identity, and two of them were performed masculinizing genitoplasty. Clitoroplasty performed in 42.3% of patients with CAH. The age distribution of the clitoroplasty was examined: 0 - <12 months, four patients, 13 months-60 months, 26 patients, > 61 patients seven patients.

Patients with ovarian dysgenesis (OD) (n:20) presented with delayed puberty (15.4±1.6 age old). Two sisters have homozygous mutation in *HAX1* (p.TRp44x). They also have sensorineural hearing loss and OD.

One patient diagnosed as ovotesticular DSD. The patient was raised as a male and had a karyotype of 46, XX.

Admission age was 14.26±1.9 years in patients with Mayer-Rokitansky-Müller-Hauser syndrome (MRKHS, n:4). Renal agenesis, pelvic kidney, mitral insufficiency and aortic stenosis, coccyx agenesis and craniostenosis were detected in patients with MRKH Type 2.

	At the admission			
46,XX DSD (n:86)	Age,	Parental consanguinity (n)	Clitoroplasty age, year	Phallus, mm
A-Disorders of ovarian development (n:21) 1-Ovarian dysgenesis (n:20) 2-Ovotesticular DSD (n:1)	15.43±1.6 years	3	-	
B-Androgen excess (n:60) a-21 hydroxylase Simple virilization (n:22)	6.75(64.7) months (0.03-82)	12	4±3.2	34.3±17
Salt wasting (n:33)	1(3.63) months (0.03-27)	21	2(1.5) (0.4-6.72)	20(40) (15-55)
b-11 b-hydroxylase (n:2) b-Aromatase deficiency (n:1) c-Other (n:2)				
C-Other 1-Müllerian Agenesis a-MRKH syndrome Type I (n:1)	14.26±1.9 year		-	
b-MRKH syndrome Type II (n:3)		2		

Conclusion:

The most common etiological diagnosis in 46 XX DSD was CAH due to intrauterine androgen exposure. However, this study showed that ovarian dysgenesis should also be considered in adolescents with puberty delay.