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CLINICAL CHARACTERISTICS OF 30 PATIENTS WITH 45,X/46,XY MOSAICISM

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Introduction: **45,X/46,XY mosaicism is a rare disease, with an incidence of 1.7/10.000 pregnancies. It is associated with a broad spectrum of phenotypes, ranging from ambiguous genitalia at birth to patients with a completely male or female phenotype. Turner syndrome stigmata and associated anomalies could be found in these patients. Patients with 45,X/46,XY mosaicism are at increased risk for germ-cell neoplasia of the gonads, especially gonadoblastoma.**

Objective and hypotheses: **To evaluate clinical presenting symptom and follow-up data of 30 patients with 45,X/46,XY karyotype.**

Methods: **Thirty patients with 45,X/46,XY mosaicism diagnosed between 1989 and 2014 in Pediatric Endocrinology Unit were reviewed retrospectively. Patients' phenotypic appearance, karyotypes, ultrasonografic and histologic findings of their gonads, hormonal activity of gonads, associated disorders and the sex of rearing were evaluated. Internal genital structures were assessed by radiological imaging and laparascopy when necessary. Basal serum testosterone levels and response to the human chorionic gonadotropin (HCG) stimulation test (1500 U HCG 3 consecutive days), laparascopy findings and sex assignment were evaluated. Chromosomal analysis was done in lymphocytes isolated from peripheral blood using conventional techniques.**

Results: **The patients' characteristics are summarized in Table 1. The mean age at diagnosis was 5.7±6.3 yrs (range:0.03-16.7). Their presenting symptoms were ambiguous genitalia (n=16), bilateral undescended testis (n=3), hirsutism and amenorrhea (n=1), amenorrhea (n=2), and short stature (n=7). One patient was diagnosed by prenatal amniocentesis; karyotype was confirmed after birth. The chromosome analysis revealed isodicentricism of the Y chromosome in 5 patients, deletions of the Y chromosome in one patient and 3 patients had 45,X/47,XYY karyotype.Sixteen children were reared as female, thirteen as male and one year old patient was undefined. Turner stigmata were found in 8 patients. Four patients (10%) had cardiac anomalies(bicuspic aortic valve, two (5%) renal anomalies(horseshoe kidney and duplicated collecting renal system), two celiac disease (5%), two Hashimoto thyroiditis (5%) and one patient bilateral conductive hearing loss.**

Bilateral gonadectomy was performed in all patients reared as female. 10 of 13 patients reared as boys underwent salpingo-hysterectomy, extirpation of streak gonad and correction of hypospadias. In 4 patients orchiopexy was done. No neoplastic changes were noted in the descended testes on ultrasound in the follow-up period.

A streak gonad and an opposite dysgenetic testis was seen in 11 cases. 8 patients had bilateral dysgenetic testes and 8 patients had bilateral streak gonads. Two patients had ovotestis on one side and dysgenetic testis on the other side. Two patients only had one gonad. Gonadoblastoma was seen in 3 patients.

Growth hormone (GH) treatment was initiated six patients (5 female, 1 male) at a mean age of 12.9±0.8 yrs (range:12.0–14.1). Mean height standard deviation score at the initiation of GH treatment of 6 patients was -4.3±1.7. Four patients reached a mean adult height of -3.4±2.6 on GH treatment.

Table 1. Some characteristics of patients with 45,X/46,XY mosaicism

Case no	Age at diagnosis (yrs)	Chief complaint	Karyotype	Gonads Right	Gonads Left	Sex of rearing
1	2.5	Ambigious genitalia	45,X/46,XY	Testis (inguinal)	Streak	F
2	12.8	Short stature	45,X/46,XY	Testis (pelvic)	Streak	F
3	0.1	Ambigious genitalia	45,X/47,XYY	Streak	Testis(inguinal)	F
4	11.8	Short stature	45,X/46,X+mar idic(Y)	Streak	Streak	F
5	0.1	Ambigious genitalia	45,X/46,XY	Testis (scrotal)	Testis(inguinal)	M
6	11	Short stature	45,X/46,XY ish idic(Y)	Streak	Streak	F
7	16.7	Short stature	45,X/46,XY	Streak	Streak	F
8	11.5	Short stature	45,X/46,XY	Streak	Streak	F
9	16	Amenorrhea Hirsutism	45,X/46,XY	Testis(pelvic)	Testis(pelvic)	F
10	2.2	Ambigious genitalia	45,X/46,XY	Testis(pelvic)	Ovotestis(pelvic)	M
11	17.5	Short stature	45,X/46,XY	Streak	Testis(pelvic)	F
12	1.5	Inguinal hernia	45,X/46,X+mar idic(Y)	Streak	Testis(scrotal)	M
13	0.6	Ambigious genitalia	45,X/46,XY	Streak	Testis(inguinal)	M
14	1	Ambigious genitalia	45,X/46,XY	Testis(scrotal)	-	Undefined
15	4.9	Cryptorchidism	45,X/46,XY	-	Testis(pelvic)	M
16	2.3	Ambigious genitalia	45,X/46,XY	Testis(inguinal)	Testis(inguinal)	M
17	0.5	Ambigious genitalia	45,X/46,XY	Testis(pelvic)	Testis(pelvic)	F
18	12.7	Cryptorchidism	45,X/46,XY idic(Y)	Streak	Streak	F
19	0.4	Ambigious genitalia	45,X/46,XY	Testis(scrotal)	Testis(scrotal)	M
20	1.5	Ambigious genitalia	45,X/46,XY	Streak	Testis(pelvic)	M
21	0.03	Ambigious genitalia	45,X/46,XY	Streak	Streak	F
22	3	Ambigious genitalia	45,X/47,XYY	Testis(inguinal)	Streak	M
23	0.25	Cryptorchidism	45,X/46,XY	Testis(pelvic)	Testis(pelvic)	M
24	16	Amenorrhea Short stature	45,X/46,XY	Streak	Streak	F
25	0.2	Ambigious genitalia	45,X/46,X del(Y)	Streak	Testis(inguinal)	F
26	0.1	Ambigious genitalia	45,X/46,X idic(Y)	Testis(scrotal)	Testis(scrotal)	M
27	3.3	Ambigious genitalia	45,X/47,XYY	Testis(scrotal)	Streak	M
28	3.9	Ambigious genitalia	45,X/46,XY	Testis(scrotum)	Testis(scrotum)	M
29	15.3	Short stature	45,X/46,XY	Streak	Testis(pelvic)	F
30	0.45	Ambigious genitalia	45,X/46,XY	Streak	Streak	F

Conclusions:

- **Although main presenting symptom of 45,X/46,XY mosaicism is ambiguous genitalia in early ages, a significant number of patients could be diagnosed with different symptoms in older ages.**
- **All patients with unilateral and bilateral undescended testis with and without hypospadias must be investigated for the presence of Müllerian structures and screened by chromosomal study.**
- **Besides follow-up for gonadal tumors, patients with 45,X/46,XY mosaicism require a clinical evaluation similar to that performed in Turner syndrome and growth velocity must be routinely followed up.**