Gonadal tumor incidence in patients with disorders od sex development containing Y chromosome or Y-derived sequences – experience from one clinical center

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Disclose statement: Nothing to disclose

Context

Risk of developing germ cell tumors (GCTs) in disorders of sex development (DSD) patients with karyotypes contain Y-chromosome or it's material (Y) increase with age. The appropriate timing for prophylactic gonadectomy in these patients is still controversial.

Objectives

The study aim was to analyze the gonadal tumor incidence, histological assessment of gonads and propose management suggestions in DSD (Y) patients who were treated in a single institution between 1997 and 07/2018.

Patients and Methods

- **16 (36.4%) with 45,X/46,XY**: 10 Turner Syndrome (TS), 6 mixed gonadal dysgenesis (MGD);
- **26 (59.1%) with 46,XY**: 15 androgen insensitivity syndrome (AIS, 9 with CAIS, 6 PAIS), 8 gonadal dysgenesis (GD) or partial GD (PGD), 1 lipoid congenital adrenal hyperplasia (CAH), 2-others
- **2 (4.5%) with 46,XX/46,XY** (*diagnosis in progress*).

Results

- 30 (68.2%) patients were reared as female (F), 14 (31.8%) as male (M);
- Gonadectomy was performed in 27(61.4%) patients: 2 *families (2 patients: TS 45X/46,XY and CAIS) refused gonadectomy*

8 Turner Syndrome DSD (Y) patients

Subjects	Age dgn (years)	BLOOD KARYOTYPE	EXTERNAL GENITALIA	Age of gonadectomy	GONADS/HISTOPATOLOGY (US: ultrasnonography; MS-Müllerian structres)
KD	0.0	45,X[38]/46,XY[62]	female genitalia	1.1	Streak gonad, fallopian tube (R, L), uterus (US)
FI	13.3	45,X[21]/46,XY[52]		14.1	Streak gonad (R, L), uterus (US)
MZ	8.6	45,X[91]/46XY[9]		9.0	Ovaries tissue, fallopian tube (R,L) uterus (US)
PN	1.2	45,X/46,XY		3.4	Gonadoblastoma (R, L), uterus (US)
JM	10.3	45,X[7]/46,XY[93]		10.9	Streak gonad fallopian tube (R, L), uterus (US)
KA	12.9	45X[73]/46,X,idic(Y)[70]		13.2	Streak gonad, fallopian tube (R, L), uterus (US)
AZ	7.8	46,X,i(X)(q10)/47, XY, i(X)(q1		8.5	Streak gonad, fallopian tube (R, L), uterus (US)
AC	5.1	45, X [38]/46,X,r(X) (p22.1q12) [12],+SRY		6.0	Leydig cell hyperplasia in the ovary (R), Streak gonad, fallopian tube (L), uterus (US)

6 DSD (Y) patients with mixed gonadal dysgenesis (45,X/46,XY MGD)

Subjects	Age dgn (years)	BLOOD KARYOTYPE	EXTERNAL GENITALIA (RT/LT – right/left gonad)	Age of gonadectomy surgery	GONADS/HISTOPATOLOGY (US: ultrasnonography; MS-Müllerian strucutres)
SA	0.0	45,X[35]/46,XY[65]	virilized	1.8	gonadoblastoma (R), ovotestis (L), uterus
OJ	1.0	45, X[12]/46, XY [18]	virilized	1.5	dysgenetic gonad – structures of testicular tssue + fallopian tube (R) , uterus (US)
LK	2.51	46,XY[44]/45,X[6]	micropenis/phllus, strocal hypospadiasis , LT + scrotum, RT(-)	0.7	MS: uterus, structures of immature testicular tissues (L, R)
SM	4.98	45,X[8]/46,XY[30]	micropenis/phallus , scrotal hypospodiasis LT – inguinal , RT (-)		dysgenetic gonad (R), MS- uterus
ZS	0.02	45X[16]/46,X+mar[14] origin - chrom Y	micropenis/phallus , hypospadiasis, RT+ abdomen (after surgery- in scrotum), LT (-)	0.9	MS: miniscule uterus and fallopian tube (L), structures of dysgenetic gonad (L)
WP	0.8	45,X[12]/46,XY[18]	micropenis/phallus , scrotal hypospadiasis, RT+ inbioscrotal folds, LT (-)	0.8	dysgenetic gonad – structures of testicular tissue (L)

13 DSD (Y) patients with 46,XY

Subjects	Age dgn (years)	DGN	EXTERNAL GENITALIA (RT/LT – right/left gonad)	Age of gonadectomy	GONADS/HISTOPATOLOGY (US: ultrasnonography; MS-Mullerian strucutres)
KK	0.1	CAIS	female genitalia	16.2	Leydig-Sertoli cell tumor (R,L); Wolffian duct (R)
KN	16.9	CAIS	female genitalia	17.2	testis (R, L); Mullerian duct (-)
KG	11.9	CAIS	female genitalia	16.8	testis (R,); Mullerian duct (-)
PO	17.3	GD	clitoromegaly	17.4	testis (R, L); Wolffian duct (R, L)
KA	14.9	GD	clitoromegaly	15.3	gonadal dysgenesis (R., L); Mullerian & Wolffian ducts (+)
SM	14.7	GD	female genitalia	15.8	gonadal dysgenesis (R, L); Mullerian duct (R, L); Leyding cells hyperplasia (L)
CK	17.7	GD	female genitalia	17.9	dysgerminoma/gonadoblastoma (L) – pT1A NX MX; gonadal dysgenesis (R);Mullerin duct (R, L)
JN	15.4	GD	female genitalia	15.5	gonadoblastoma/dysgerminoma (L); gonadal dysgenesis (R); Mullerian duct (R, L)
CKL	17.2	GD	female genitalia	17.4	carcinoma embryonale (60%), Yolk sack tumor (40%) (L); gonadoblastoma (R)
NB	1.8	PGD?	posterior labioscrotal fusion, R&L gonad in l-s: 6 points in EGS	2.2	testis (L), no Mullerian ducts
GZ	0.1	PGD?	Prader II/III	12.9	testicular tissues + Leydig cell hyperpasia+ gynandroblastoma (R) ovary tissue+Mullerian& Wolffian duct + dysgerminoma (L)
OM	6.8	GD?	Female genitalia	7.8	ovarian tissue +Mullerian duct (R, L)
WJ	10.6	Lipoid CAH	Female genitalia	11.0	testicular tissues (R, L)

Conclusions

- The overall GCTs risk was **25.9%** and 46,XY GD carried the highest risk.
- Optimal protocol in the management of DSD is still controversial. Therefore further search for useful clinical/lab markers of individual tumor risk is urgently needed.