Do Males with 45,X/46,XY Mosaicism Have Turner Syndrome

Michelle Knoll

Research Abstract Title

Submitting/Presenting Author (must be a trainee): Michelle Knoll, MD
Primary Email Address: mmknoll@cmh.edu

☐ Medical Student
☐ **Resident/Psychology Intern (≤ 1 month of dedicated research time)**
☐ Resident/Ph.D/post graduate (> 1 month of dedicated research time)
X Fellow

Primary Mentor (one name only): Jill Jacobson, MD
Other authors/contributors involved in project: Julie Strickland, MD

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Describe role of Submitting/Presenting Trainee in this project (limit 150 words):
Dr. Knoll conceptualized this subanalysis, collected the data, ran the data analysis, and wrote the abstract draft. Dr. Jacobson assisted in the conceptualization of the project, reviewed data analysis, and edited the abstract. Dr. Strickland assisted in the conceptualization of the project and reviewed the abstract.

Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words

Background:
Patients with 45,X/46,XY mosaicism can have genitalia spanning the range from typical female to typical male, and the sex assigned at birth is often based on the appearance of the genitalia. According to current nomenclature, only the subgroup assigned female are diagnosed with Turner syndrome (TS) (Gravholt et al, 2017). Clinical practice guidelines recommend that girls with TS be screened for several comorbidities, including short stature, cardiac and renal anomalies, and autoimmune conditions, but there are no recommendations for screening of boys with 45,X/46,XY mosaicism.

Objectives/Goal:
We sought to determine if boys with 45,X/46,XY mosaicism exhibited a similar rate of comorbidities commonly seen in girls with TS.

Methods/Design:
We did a retrospective review of patients with 45,X/46,XY mosaicism seen in our multidisciplinary Differences of Sex Development Clinic. A total of 22 patients (14 raised as female, 8 raised as male) were identified. Results of cardiology, renal, audiology, and thyroid screening were recorded for all subjects, along with celiac screen for subjects older than age 2 years, and A1c, liver function, and vitamin D for subjects older than age 10 years. Height z-score based on sex of rearing before starting growth hormone was obtained. One female subject with

congenital adrenal hyperplasia was excluded from height analysis. Data were analyzed using Mann Whitney U and Chi-Square via SPSS (Version 27, IBM).

Results:

Although female subjects were significantly more likely to have screening tests performed (92/102 vs 37/58, $p<0.001$), there was no significant difference in the number of abnormal screens between male (6/37, 16%) and female (10/92, 11%) subjects, $p=0.405$. Five male subjects (62.5%) had cardiac conditions compared to 11 female subjects (78.5%), both of which are higher than the general population estimate of 1%. One male subject (12.5%) had a serious cardiac condition (hypoplastic left heart syndrome). All subjects had height z-score below the mean for sex. Z-scores were not significantly different between male (median -2.57, -3.78 to -0.59) and female subjects (median -1.7, -3.20 to -0.54), $U(21) = 33$, $z = -1.376$, $p=0.185$.

Conclusions:

Our data suggest that males with 45,X/46,XY mosaicism have similar rates of comorbidities compared to females with TS with the 45,X/46,XY genotype. The data suggest the need for a multicenter registry to expand these findings. Screening males according to the TS Clinical Practice Guidelines may allow early recognition of comorbidities.