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Diagnostic and Perinatal Features of Turner Syndrome with Trisomy X Mosaicism: An InsighTS Study

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Please state why this abstract is "late-breaking"

The InsighTS Registry is a recently created clinic-based registry currently open for enrollment at 6 national centers. At the time of the regular abstract deadline, we had insufficient numbers of participants enrolled to conduct any relevant analyses. Enrollment and data entry completion have greatly improved over the last two months allowing us to compare diagnostic and perinatal features of girls with mosaic 45,X/47,XXX (n=18) to other TS karyotypes. This represents the largest cohort of girls with 45,X/47,XXX in the literature. We do anticipate having a couple more 45,X/47,XXX participants by the time of the PES meeting and we will plan to include those with updated analyses.

Objectives

Turner Syndrome (TS) occurs in ~1 in 2000 females who have partial or complete absence of the second sex chromosome. TS may occur with mosaicism for 46,XX (~20% of TS) and/or 47,XXX (~3% of TS) cell lines. Literature on mosaic 45,X/47,XXX are limited to case reports and series. The aim of this study was to describe the phenotype of 45,X/47,XXX and compare to non-mosaic TS (45,X) and mosaic for an XX cell line (45,X/46,XX).

Methods

The InsighTS Registry has prospectively enrolled 246 females with TS (11.5±9.5 y of age) from six institutions across the US and obtained TS diagnostic, birth, and neonatal histories from medical records. Those with 45,X/47,XXX (n=18), 45,X/46,XX (n=32), and 45,X (n=87) were included in this retrospective analysis. All three karyotype groups were compared using ANOVA for continues variables and Chi-squared for categorical variables; pairwise comparisons were conducted when group differences were significant ($\alpha<0.05$).

Results

Seven percent (7%) of the InsighTS cohort had mosaicism for trisomy X, 33% of which were identified prenatally (Table 1). Age of TS diagnosis was older in those with trisomy X mosaicism (7.4±5.0 y) compared to those with 45,X (2.7±3.6 y; $p<0.001$), but not different from

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45,X/46,XX (p=0.2). Indications for postnatal genetic testing were different between groups, but not for prenatal testing (Chi-Square 31.5, p=0.002). In pairwise comparisons, 45,X/47,XXX was more likely to be diagnosed secondary to delayed puberty/amenorrhea (17%) and short stature (67%) and less likely to be diagnosed secondary to dysmorphic features (0%) or congenital anomaly (0%) when compared to non-mosaic TS ($p<0.05$ for all), however proportions were similar to 45,X/46,XX ($p>0.05$). Maternal age at birth differed between groups (ANOVA p= 0.003), however 45,X/47,XXX (30.4±3.5 y) did not differ from monosomy X (28.0±5.7 y) or 45,X/46,XX (32.8± 5.4 y) groups ($p>0.05$). Gestational age, birth length, and birthweight did not differ between groups. While there were trends toward fewer neonatal complications in 45,X/47,XXX, only presence of lymphedema (0% in 45,X/47,XXX vs 33% in 45,X, p=0.02) reached significance.

Conclusions

This retrospective analysis of 18 girls with 45,X/47,XXX showed similar reasons for postnatal diagnosis and perinatal history to those with 45,X/46,XX, but differed from those with monosomy X. Future directions include assessment of medical and psychological comorbidities in 45,X/47,XXX.

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