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Genetic counseling for women with 45,X/46,XX mosaicism: Towards more personalized management

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Abstract

Despite numerous clinical series, consistent karyotype-phenotype correlations for Turner syndrome have not been established, although a lower level of 45,X is generally thought to be associated with a milder phenotype. This limits personalized counseling for women with 45,X/46,XX mosaicism. To better understand the phenotypic spectrum associated with various levels of 45,X/46,XX mosaicism, we compared patients evaluated in the Massachusetts General Hospital Turner Syndrome Clinic to determine if cardiac, renal, and thyroid abnormalities correlated with the percentage of 45,X cells present in a peripheral blood karyotype. of the 118 patients included in the study, 78 (66%) patients had non-mosaic 45,X and 40 (34%) patients had varying levels of 45,X/46,XX mosaicism. Patients with ≤70% 45,X compared with those with >70% 45,X had a significantly lower frequency of cardiac and renal anomalies. The presence of hypothyroidism was somewhat lower for the ≤70% 45,X group, but was not statistically significant. Supplemental tissue testing on another tissue type, typically buccal mucosa, was often useful in counseling patients with 45,X mosaicism. Given the modest sample size of patients with varying levels of mosaicism and the variability of Turner syndrome abnormalities, we hope this preliminary study will inspire a multicenter collaboration, which may lead to modification of clinical guidelines. Because several patients with ≤70% 45,X were ascertained from perinatal care referrals, we still advise women with 45,X mosaicism pursuing pregnancy to receive standard Turner syndrome cardiac surveillance. There is an opportunity to personalize counseling and surveillance for patients based on percentage of 45,X cells on chromosome analysis.

Keywords: Congenital heart defects; Counseling techniques; Genetic counseling; Karyotype; Risk management; Sex chromosome aneuploidy.

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