CLINICAL VIGNETTE

A Case of Mosaic Turner Syndrome: Rare Cause of Amenorrhea

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Case Presentation

A 35-year-old female with no significant past medical history presented to the Internal Medicine clinic with amenorrhea. The patient reports a negative urine pregnancy test three weeks ago. Usually her menstrual cycles are regular, occurring every 25 days and lasting 3 to 5 days. However, she has not had a period for the past 3 months. She denied associated symptoms other than mild hair loss and denied no recent changes in exercise pattern, stress, weight loss, acne, and hirsutism. She is married and has two healthy children, ages 16 and 10 years old.

On exam, vital signs were T 36.2 °C, BP 118/81, HR 79, SpO2 97%, height 5'4", weight 130 lbs. Physical exam was notable for a healthy appearing woman of average stature and normal development. She had mild tenderness to palpation in the lower abdomen though otherwise unremarkable. Labs were sent including Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH), Prolactin, Thyroid Stimulating Hormone (TSH) with reflex T4, DHEA-Sulfate, Testosterone, Total Beta hCG, Complete Blood Count, and Comprehensive Metabolic Panel. Lab work was notable for elevated FSH at 39.3 mIU/mL, negative pregnancy test, and normal estradiol level of 47 pg/mL. Pelvic ultrasound was unremarkable. Given concern for primary ovarian insufficiency, the patient was referred to Obstetrics and Gynecology.

On initial consultation with OB-Gyn, FSH and estradiol were repeated, and Karyotype, FMR1 gene permutation test, and adrenal antibodies were also sent. Repeat FSH testing was normal at 19 mIU/ML and estradiol level was normal 79 pg/mL. Adrenal antibody was negative but Karyotype showed results 45,X/46,XX, consistent with mosaic Turner syndrome.

Discussion

Turner syndrome affects 25-50 per 100,000 females, with mosaic Turner syndrome 45,X/46,XX making up 15–25 % of these cases.[1] The features of classic Turner syndrome include short stature, a webbed neck, broad chest and ovarian insufficiency.[2,3] A few indications for chromosome analysis include women with unexplained delayed puberty or menarche, infertility, idiopathic short stature, obstructive left-sided congenital heart defect, and hearing impairment for women less than 40 years of age.[1] Patients with Turner mosaicism 45,X/46,XX have a milder phenotype, including less prevalent congenital heart disease and are more likely to have spontaneous menstruation and pregnancies.[2] Turner mosaicism may go undiagnosed or diagnosed later in life given milder phenotype.

Tuke et al, studied 244,000 adult women to assess X chromosome aneuploidy phenotypes. Two hundred and sixteen individuals were found to have mosaic Turner syndrome, which is a higher prevalence than reported in other studies. Out of the women who tested positive for mosaic Turner syndrome, none reported having Turner syndrome at the initial visit. These individuals reported mean menarche timing was 13.2 years, not different from the mean age of 12.95 in the 46,XX women.[4] Most of the mosaic cases reported a pregnancy with no increased incidence of pregnancy loss. Ninety-five of the 45,X/46,XX mosaic women reported a natural menopause age, while the rest in the study were not at an age of menopause or did not report age of menopause. The women with mosaic Turner syndrome 45,X/46,XX did not have a higher incidence of cardiac operations and were not more likely to be on blood pressure medication than the 46,XX women.[4]

Many patients with mosaic Turner syndrome do not undergo chromosomal analysis given mild phenotype. In comparison to classic Turner syndrome, Tuke et al reported women with mosaic Turner Syndrome 45,X/46,XX were average height, had a normal reproductive lifespan and birth rate, and no reported cardiovascular complications.[4] This study was biased in favor of healthier individuals with a more benign phenotype. Therefore, patients with mosaic Turner syndrome should still be evaluated by Genetics and undergo recommended screenings.

In this case, our patient reported normal menstrual history, normal pregnancies and delivery of two healthy children up until she developed secondary amenorrhea at age 35 years and was diagnosed with mosaic Turner syndrome. She lacked the other classic phenotype characteristics seen in Turner syndrome. Interestingly, at 6-month follow-up, our patient reported that she had started menstruating regularly again. Given her subtle presentation, the diagnoses could easily have been missed.

Unfortunately, literature shows that delays in diagnosis are found with all forms of Turner syndrome. The phenotypic presentation of Turner syndrome may be subtle and variable.[5] Primary care physicians should be vigilant and consider sending karyotyping for patients who are short in stature (more than 2 standard deviations below the mean) or present with

unexplained amenorrhea or infertility. Once diagnosed, the primary care physician should coordinate with multiple specialties to ensure the best care for this high-risk population.

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