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An Uncommon Variant of Turner Syndrome in an African American Woman

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Abstract

The extra gonadal consequences of Turner's Syndrome (TS) also pose risks to patients, namely cardiovascular. Clinicians should maintain a level of clinical suspicion for TS in patients with primary amenorrhea even without typical physical characteristics. Interestingly, TS has uncommon variant forms with varying degrees of clinical manifestations. Even so, all TS and TS variants maintain a high risk for cardiovascular events. Therefore, early TS diagnosis is of utmost importance. Here, we present a case of a young, African-American woman with primary amenorrhea with few overt clinical signs of TS. With high clinical suspicion, genetic testing is pursued and demonstrates the TS variant. This is important because variant forms have a similar increased risk of premature hypertension, diabetes, and aortic dissection.

Keywords

Turner Syndrome, Turner Syndrome Variant, Primary Amenorrhea, Isodicentric X Chromosome

1. Introduction

Turner's Syndrome (TS) results from a partial or complete structural abnormality of the X chromosome [1]. The clinical manifestations include gonadal dysgenesis, hearing difficulties, skeletal abnormalities, short stature, cubitus valgus, cardiac defects including bicuspid aortic valve and coarctation of the aorta, learning disabilities, and visuospatial defects. The prevalence of TS is approximately 1/2500 women [2]. It is important to note that while the genotype of most TS women is 45 XO, there are a host of other structural chromosomal abnormalities including isochromosomes, rings, a Y chromosome, and mosaicism.

While more than 60% of TS cases are due to X monosomy, isodicentric (idic) X chromosomes are not common [3]. Isochromosomes form when one arm of

the chromosome is lost and the remaining arm is duplicated. This creates either two short arms or two long arms now joined and the presence of two centromeres [4]. The result is an idic chromosome. Diagnosing TS in patients with idic X can pose a challenge because phenotypes may vary. Tsu *et al.* report a case of a woman with idic X without any typical features of TS. Thus, it remains important to have a high level of suspicion in women with primary amenorrhea as TS and its variants all have an increased risk for cardiac events [5] [6].

We present a case of a 22-year-old woman diagnosed with a TS variant presenting with primary amenorrhea and few TS features. Genetic testing revealed the presence of an idic X chromosome. Irrespective of TS genotypic variants, cardiovascular ramifications remain. We discuss the diversity of phenotypes in TS variants and thus the importance of high clinical suspicion for TS.

2. Case Report

An otherwise healthy 22-year-old woman came to the women's clinic for a routine gynecological exam and Sexually Transmitted Disease (STD) screening. She never had menses and her primary amenorrhea was never evaluated. She is sexually active.

Her past medical history was non-contributory and her birth was uncomplicated and at term. There was no pertinent surgical or family history. She denies ever being pregnant. She gives a history of tobacco use; she denies alcohol or drug use.

Review of systems negative for galactorrhea, decreased appetite, weight loss, or weight gain. Review of systems positive for primary amenorrhea, vaginal discharge, and a genital rash.

On examination, her vitals were within normal limits. Her BMI was 35.19. Her height was four feet and 10 inches. She was a petite woman with supple neck. Breast exam demonstrated breasts at Tanner Stage II.

On pelvic exam, her external genitalia were normal in appearance, except for a slightly prominent clitoris. A speculum exam revealed a normal cervix, but the size of the uterus could not be appreciated on bimanual exam. Her laboratory results are shown in **Table 1**.

STD testing and nuswab panel (tests for vaginitis such as Bacterial vaginosis, Trichomonas, and Candida species) were negative. Pap smear demonstrated no abnormal cells.

Pelvic ultrasound showed a normal uterus without thickened stripe and normal ovaries (**Figures 1-3**). Cytogenetic karyotyping revealed 46, X, idic (X) (p 11.2) with a normal X chromosome and the other X only composed of two long arms.

Our patient was counseled on genetic findings and started on combined oral contraception and vitamin D supplement. She was referred to Primary care, endocrinology, and cardiology for initial evaluation. She has not followed up in cardiology or endocrine clinic. Her primary care physician started her on Losartan.

Table 1. Laboratory investigations.

Test	Result	Reference range
Estradiol	Less than five pg/ml	Post menopausal if less than 6
LH	30.0 mIU/mL	Post menopausal if 7.7 - 58.5 mIU/mL
FSH	57.4 mIU/mL	Post menopausal if 25.8 - 134.8 mIU/mL
Testosterone, free	1.8 pg/ml	0.0 - 4.2
Prolactin	4.4 ng/mL	4.8 - 23.3 ng/mL
TSH	2.6 uU/mL	0.45 - 4.5 uU/mL

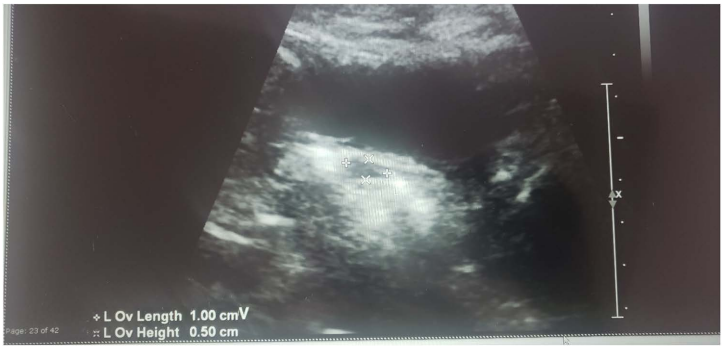

Figure 1. Left ovary, sagittal view.

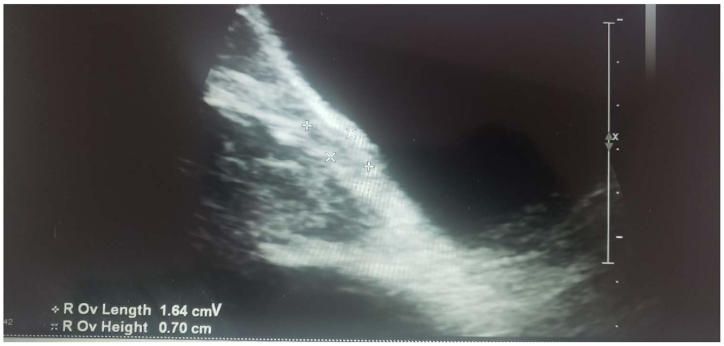

Figure 2. Right ovary, sagittal view.

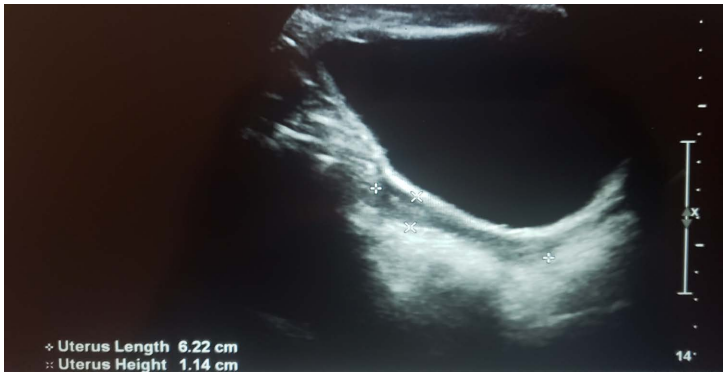

Figure 3. Uterus, saggital view.

3. Discussion

Idic X chromosomes comprise roughly 18% of all TS cases and the idic Xp11

remains the most common isochromosome seen in humans [7]. While the exact pathogenesis remains poorly understood, there are some areas of the genome that are common breakpoints. This leads to breaks seen in the p arm. This essentially leads to monosomy although there may still be paucity of p material. The two q arms form what is termed an idic X chromosomes. Thus, the karyotype 46 X idic X (p 11.2), as seen in our patient.

Our patient was short and had immature breast development (Tanner stage II). However, her primary amenorrhea and labs consistent with ovarian insufficiency (not unlike that of postmenopausal woman) provided enough suspicion for underlying TS. Recognize that TS can present across a spectrum given the genotypic variants of TS. In fact, patients with identical karyotypes have been found to have varying clinical manifestations [4].

Characteristic TS features include short stature, cubitus valgus, webbed neck, broad chest with widely spaced nipples, lymphedema, hearing impairments, and evidence of premature ovarian failure. **Pettigrew *et al.* report a 28 year woman with short neck, short stature, highly arched palate, low posterior hairline, broad chest, and widely spaced nipples, and amenorrhea found to have 46, X, idic [8].

The clinical manifestations for idic TS patients may not always be so overt. For instance, a 21 year old Taiwanese woman was found to have idic TS with 46, X, idic (X) (q22) and her only presenting features included short neck and amenorrhea [3]. Similarly, in report by Chan *et al.* who discuss a teenager who presented only with short stature and absent puberty. Workup demonstrated cell line with monosomy X as well as normal X and idic Xp11q28 and incidental finds of Celiac disease and hypothyroidism [2]. Yu *et al.* summarized it well: cytogenetic abnormalities in TS are more important than the somatic stigmata [3].

Despite the challenges in recognizing TS given their diverse phenotypes, TS patients remain quite homogenous in their increased risk for metabolic syndrome [9] and should be followed by a primary care physician. Approximately, one-third of all TS patients will have a cardiac malformation [6]. TS women have a 100-fold increased risk of aortic dissection compared to non-TS women [4]. They should have screening transthoracic echocardiogram and Electrocardiogram (ECG). Cardiac MRI should be done every 5 to 10 years [6].

4. Conclusion

TS usually presents as females with short stature, gonadal dysgenesis, and 45, X cell line that is either singly or in combination with another mosaic cell line (7). Our patient presented with short stature and amenorrhea. Our case demonstrates the phenotypic diversity of patients with TS and highlights their uniform risk for cardiovascular events. Thus, it remains important to have a high level of clinical suspicion and check a karyotype.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

**Sometimes patients have overwhelming phenotype suggestive of TS.

References

[1] Liang, L., Mei, L., Shi, Y., *et al.* (2021) Turner Syndrome with Xp Deletions and Rare Endometrial Abnormalities: A Case Report. *Medicine* (*Baltimore*), **100**, e27571. https://doi.org/10.1097/MD.0000000000027571

[2] Chan, J.T. and Cabanas, M.C.C. (2021) A Rare Variant of Turner Syndrome with Isodicentric X Chromosome Resulting in Trisomy: A Case Report. *Journal of the Endocrine Society*, **5**, A695-A696. https://doi.org/10.1210/jendso/bvab048.1417

[3] Yu, T.Y., Lin, H.S., Chen, P.L. and Huang, T.S. (2015) An Isodicentric X Chromosome with Gonadal Dysgenesis in a Lady without Prominent Somatic Features of Turner's Syndrome. A Case Report. *Journal of the Formosan Medical Association*, **114**, 77-80. https://doi.org/10.1016/j.jfma.2011.05.011

[4] Shahriar Salamat, M. (2010) Robbins and Cotran: Pathologic Basis of Disease, 8th Edition. *Journal of Neuropathology & Experimental Neurology*, **69**, 214. https://doi.org/10.1097/NEN.0b013e3181cd8dbc

[5] Chou, Y.Y., Wang, C.J., Lin, C.H., Chung, H.T. and Lo, F.S. (2020) Association between Cardiovascular Anomalies and Karyotypes in Turner Syndrome Patients in Taiwan: A Local Cohort Study. *Pediatrics and Neonatology*, **61**, 188-194. https://doi.org/10.1016/j.pedneo.2019.10.001

[6] Morgan, T. (2007) Turner Syndrome: Diagnosis and Management. *American Family Physician*, **76**, 405-410.

[7] Scott, S.A., Cohen, N., Brandt, T., Warburton, P.E. and Edelmann, L. (2010) Large Inverted Repeats within Xp11.2 Are Present at the Breakpoints of Isodicentric X Chromosomes in Turner Syndrome. *Human Molecular Genetics*, **19**, 3383-3393. https://doi.org/10.1093/hmg/ddq250

[8] Pettigrew, A.L., McCabe, E.R., Elder, F.F. and Ledbetter, D.H. (1991) Isodicentric X Chromosome in a Patient with Turner Syndrome—Implications for Localization of the X-Inactivation Center. *Human Genetics*, **87**, 498-502. https://doi.org/10.1007/BF00197176

[9] Ranke, M.B. and Saenger, P. (2001) Turner's Syndrome. *The Lancet*, **358**, 309-314. https://doi.org/10.1016/S0140-6736(01)05487-3