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Case Report

Atypical genotype in a typical phenotype

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Abstract:

Introduction: Usually, onset of thelarche heralds puberty. Delayed puberty is worrisome and needs medical attention. Our patient in her late adolescence presented with primary amenorrhea, whose evaluation left us surprised.

Case report: An eighteen-year-old scholastically backward girl, presented with complaints of not attaining menarche. Physical examination included a height of 156 cm(10^{th}-25^{th}centile),weight 51 kg(50^{th} centile), wide carrying angle, multiple nevi and a broad chest, however no other Turner stigmata was noted. Her sexual maturity rating (SMR) was $A_2P_2B_1$ Laboratory investigations revealed increased gonadotropins (FSH:77mIU/ml; LH:25.4mIU/ml), low estradiol (14 pg/ml) and vitamin-D deficiency (21ng/ml). Ultrasonography of abdomen-pelvis showed small infantile uterus with streak ovaries. Karyotype (50 metaphases) demonstrated mosaicism [47,XXX (29)/45,X(19)/46,XX(2)]. Hormone replacement therapy and vitamin

D replacement was initiated.

Conclusion: 30-40% of the Turner syndrome are mosaics, the most common being 45,X/46,XX. Mosaicism is the presence of 2 or more cell lines with different chromosomal constitutions. The cell lines are derived due mostly to postzygotic mitotic nondisjunction. X/XX/XXX can present with or without classical turner stigmata. Trisomy X has a spectrum of presentation from normal menses and fertility to recurrent abortions and primary/secondary amenorrhea (primary ovarian insufficiency). Varied clinical phenotype due to three cell lines in a Turner mosaic makes this case unique.

Keywords: turner syndrome; trisomy x; mosaic turner syndrome; three cell lines; 47,XXX/46,XX/45,X

Introduction:

Puberty in females is determined by the onset of thelarche. Whenever an adolescent girl presents with short stature, primary amenorrhea and absence of secondary sexual characteristics, the first diagnosis which comes to our mind is Turner syndrome (TS). It affects approximately 1 in 2,500 live female births [1]. This syndrome occurs due to either monosomy X (the most common form of TS with the classical phenotype) resulting from meiotic nondisjunction in the parental gamete or in the early embryonic divisions (the latter causing mosaicism). The severity of clinical manifestations is related to the type of chromosomal abnormalities, the time at which chromosome disjunction occurred and the proportion of compromised cells in each tissue [2]. Here we present to you a case of an adolescent female who presented with primary amenorrhea, with a not-so classical genotype.

Case report:

18 year old adolescent girl, presented with primary amenorrhea with poor development of secondary sexual characteristics. She was born to a non-consanguineous wedlock and was the 7^{th} child of 8 children. No history of delayed puberty in any family member or decreased sense of smell. Academically, she was a school dropout and preferred helping her mother at home. On examination her vitals were stable with no hyper/hypotension. She weighed 51 kg (50^{th} centile), was 156 cm (10-25^{th} centile) tall and with normal body proportions. She had specific Turner stigmata which included a broad shield-like chest, wide spaced nipples, a wide carrying angle, multiple nevi (10 in number) and bilateral fifth finger clinodactyly. Her sexual maturity rating as per Tanner classification was $A_2B_1P_2M_0$. She had no cardiac murmur, no goiter, normal neck length, no evidence of brachydactyly. In view of some of the clinical features of Turner syndrome and the primary amenorrhea laboratory investigations (Table 1) and a Karyotype evaluation (Figure 2) was done. The laboratory investigations proved that the child was having primary ovarian insufficiency (FSH levels were menopausal with low estradiol) and vitamin D level insufficiency. The sonogram of the pelvis showed an infantile uterus with streak gonads. The karyotyping left us amazed with the presence of 3 cell lines(47,XXX/46,XX/45,X), majority of which was 47,XXX. The treatment was hormone replacement therapy with estradiol valerate and Vitamin D supplementation.

Figure 1: *Index patient with absent secondary sexual characteristics, shield like chest and wide spaced nipples.*

Investigations	Results
Free T4 ng/dl	1.12 (0.8-2.2)
TSH mIU/ml	5 (0.5-5.5)
LH mIU/ml	25 (menopausal range)
FSH mIU/ml	77 (menopausal range)
Estradiol pg/ml	14 (<15:prepubertal)
Serum Calcium (mg/dl) Serum Phosphate (mg/dl) ALP IU/l	9.6 (9-11) 4 (2.5-4.5) 133 (20-140)
Vit D ng/ml	21 (21-30 insufficient)
USG abdomen and pelvis	Infantile uterus with streak gonads No renal anomalies
Thyroid antibodies(Anti-Thyroid peroxidase and Anti Thyroglobulin)	Negative
Bone Age	15.2 years (RUS TWIII) Delayed by 3 years
2D echo	Normal

(RUSTWIII) = RADIUS-ULNA STAGING TANNER WHITE 3

Table 1: *Laboratory and radiological investigations of the patient.*

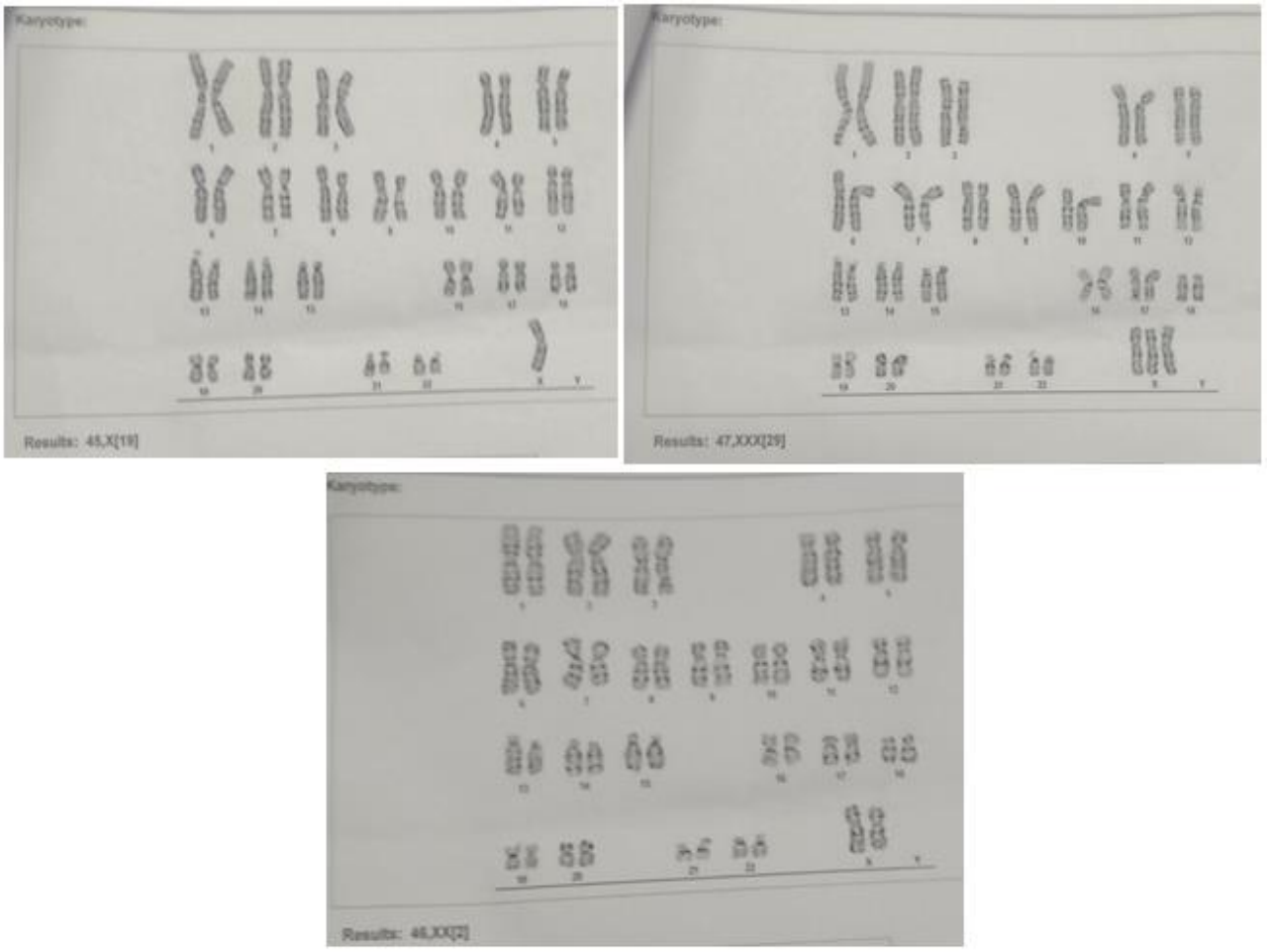

Figure 2: *The karyotyping (GTG banding) in which 50 metaphases counted revealed mos 47,XXX[29]/45,X[19]/46,XX[2]*

Discussion

Trisomy X (47,XXX) is a sex chromosome disorder with a variable phenotype, incidence being 1 in 1,000 female births [3].This de-arrangement also occurs due to meiotic non-disjunction, the risk increasing with maternal age. The most common physical features include normal to tall stature, epicanthal folds, occasional hypotonia and clinodactyly. Seizures, genitourinary abnormalities, learning disabilities (verbal processing defects, decrement in IQ and global delays) and motor delays are also seen. The pubertal onset can be normal or delayed and fertility can range anywhere from being normal to premature ovarian failure [4, 7]. Birthweight and length are usually normal for gestational age, however, stature increases in early childhood and by adolescence most girls with 47,XXX are at or above the 75th percentile for height [8]. On the other hand, Turner Syndrome is characterized cytogenetically by X chromosome monosomy, the presence of an abnormal X chromosome (isochromosome/ring chromosome/Xp or Xq deletion) or mosaicism of a 45,X cell line with another cell line. Mosaicism(45,X/46,XX or 45,X/47,XXX cell lineages) has been detected in 30% of the Turner syndrome cases [4,6,7].This condition has classical phenotypical features with short stature, delayed puberty, ovarian dysgenesis (hypergonadotropic hypogonadism), infertility, congenital malformations of the heart, hearing loss, ocular problems, endocrine disorders such as type 1 and type 2 diabetes mellitus, osteoporosis and autoimmune disorders [5]. The clinical presentation in our case was typical of a Turner phenotype which is consistent with gonadal dysgenesis causing primary amenorrhea, however the absence of short stature could be attributed to the huge proportion of the trisomy X(47,XXX) cell line. Although hypergonadotropic hypogonadism is a known entity in Turner syndrome, there are case reports of primary ovarian insufficiency in Trisomy X also. Since the height of the patient was normal compared to the mid-parental height, medical attention was never sought for short stature and the girl presented to us only because she had not attained menarche. Cases with X/XX/XXX have been described to report in adult life, during evaluation of recurrent pregnancy loss and short stature accounts for only 14% of diagnoses. Similarly, there have been case reports, albeit few, of triple mosaic TS with spontaneous pubarche, thelarche, and menarche [6].

Conclusion

This harps the fact that any adolescent presenting with delayed puberty has to be evaluated with a karyotype, even if she has classical Turner stigmata. Mosaicism is the one entity which will decide the age and the mode of presentation. More so, it is all the more essential for the karyotype in any patient with primary amenorrhea to look for Y cell line so as to prevent a gonadoblastoma in future. Appropriate genetic counselling has to be provided to these patients as aneuploidy in off-springs and its consequences is a possibility. Trisomy X has a heterogenous presentation from normal menses, tall stature and normal fertility to recurrent abortions and primary/secondary amenorrhea (primary ovarian insufficiency). A mixed phenotype in our case due to

three cell lines (Triple mosaic TS) in varying proportions makes this case unique.

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Conflict of interest: None

References

1. Gravholt CH et al. (2017) International Turner Syndrome Consensus Group. Clinical practice guidelines for the care of girls and women with Turner syndrome: proceedings from the 2016 Cincinnati International Turner Syndrome Meeting. Eur J Endocrinol. Sep;177(3):G1-G70.
2. Saenger P, Wikland KA, Conway GS, Davenport M, Gravholt CH, Hintz R, et al. (2001) Recommendations for the diagnosis and management of Turner syndrome. J Clin Endocrinol Metab. 86:3061–3069.
3. Tartaglia, N.R., Howell, S., Sutherland, A. et al. (2010) A review of trisomy X (47,XXX). Orphanet J Rare Dis 5, 8.
4. Sybert VP. (2002) Phenotypic effects of mosaicism for a 47,XXX cell line in Turner syndrome. Journal of Medical Genetics. 39:217-220.
5. Classic pages in obstetrics and gynecology by Henry H. (1938) Turner. A syndrome of infantilism, congenital webbed neck, and cubitus valgus. Endocrinology, vol. 23, pp. 566-574. American journal of obstetrics and gynecology.
6. Brambila-Tapia AJ, Rivera H, García-Castillo H, Domínguez-Quezada MG, Dávalos-Rodríguez IP. (2009) 47,XXX/45,X/46,XX mosaicism in a patient with Turner phenotype and spontaneous pubertal development. Fertil Steril. Nov;92(5):1747.e5-7.
7. Linden MG, Bender BG, Harmon RJ, Mrazek DA, Robinson A. (1988) 47,XXX: what is the prognosis? Pediatrics. 82 (4): 619-630
8. Phenotypic effects of mosaicism for a 47,XXX cell line in Turner syndrome Journal of Medical Genetics. (2002) 39:217-220.

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