Volume-4, Issue-6, June-2015 • ISSN No 2277 - 8160

Research Paper | Medical Science

From Menstrual Cycle Anomalies to Turner's Syndrome Variant: Case Report

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ABSTRACT

This paper is a case report of a teenager female who was incidentally found with Turner syndrome mosaicism (45 XO/ 46 XX) after a few episodes of metrorrhagia. Although no uterine, neither ovarian anomalies were found she was checked for all the potential complications as seen in complete classical phenotype and she was found (a part from short stature of 143 centimeters) with hypothyroidism, vitamin D deficiency, bicuspid normal functioning aortic valve, and some audiogram defects. None of these were previously known or recognized before by the patient. The menses became normal within months after a 3 months cycle of 10 days monthly progestative. Levothyroxin, vitamin D and calcium supplements were initated. Lifelong follow-up is necessary.

KEYWORDS : Turner syndrome, genetic mosaicism, nanism, metrorrhagia

Introduction

Turner syndrome is a genetic (chromosomal) condition associated with 45 XO karyotype (monosomy). Despite the classical phenotype features the diagnosis might be missed especially in cases with genetic mosaicism as 45 XO/ 46 XY (with Y line) or 45 XO/ 46 XX (with normal female karyotype line). (1,2,3) Probably the most common characteristic is the short stature which is need to be treated (before the growth cartilage are closed) with high doses of growth hormone although the causing defect is related to the short stature homeobox-containing (SHOX) gene. (1,2,3) The others elements in Turner syndrome apart from nanism are delayed puberty/primary amenorrhea, cardiac anomalies especially in aortic valve (and high cardiovascular risk), kidney anomalies, ear/nose anomalies. (4,5) The endocrine panel is focused on (apart from gonads anomalies) higher risk of Hashimoto's thyroiditis, insulin resistance and vitamin D deficiency / osteoporosis. (4,5,6,7)

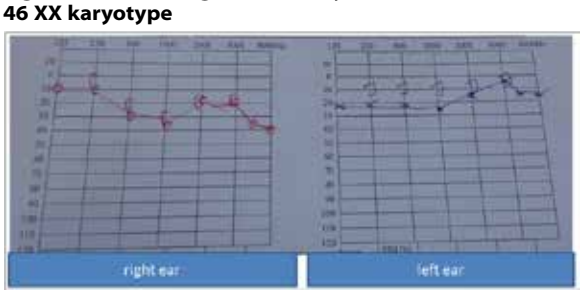
Aim

This is brief case report regarding a teenager female accidently diagnosed with Turner's syndrome variant.

Case presentation

17-year old female subject with normal apparent phenotype had menarche at age of 12 years old and monthly regular menses up to the present. For the last 3 months she presented metrorrhagia so she had a few tests done: both the haematological and gynaecological exams were normal. She decided to look for a second opinion this time from an endocrinologist point of view. The endocrine evaluation found short stature of 143 centimetres (cm) and enclosed growth cartilages. Because of height the karyotype was performed and found 45 XO/ 46 XX. The abdominal computed tomography was performed and uterus, ovaries and kidney were normal shaped. We checked the ear and the audiograme found two frequencies there were hardly detectable by the patient but she previously did not know about this aspect. (Figure 1)

Figure 1. The audiogram in a 17-year female with 45 XO/ 46 XX karyotype



The cardiac examination pointed bicuspid aortic valve with normal function up to the moment of evaluation. Autoimmune hypothyroidism is found based on TSH level of 20 μIU/mL with normal ranges between 0.4-4.5 μUI/mL. Negative thyroid antibodies were pointed but hypoecogenic thyroid ultrasound pattern was suggestive for chronic thyroiditis. Levothyroxine was started from daily 25 μg with progressive increase dose based on TSH. The 25-hydroxyvitamin D was low of 4 ng/mL with normal levels between 30 and 100 ng/mL with negative blood tests for celiac disease. No osteoporosis was found. Vitamin D and calcium supplements are introduced. The menses normalised within 3 months with 10 days monthly progestative. Lifelong follow-up is recommended.

Discussion

This case highlights the importance of paying attention to the short stature phenotype. Although in this case the growth cartilages were closed and the patient could not beneficiate of growth hormone therapy the diagnosis is essential to be established regardless the patient's age. The Turner syndrome variant with normal female genotype line is the explanation of normal pubertal and gonads development. This allows future fertility. (8,9) This situation is opposite to the XY line mosaicism when gonadectomy is recommended in order to lower the risk of gonadoblastoma. (8,9)

The patient in this case has some cardiac anomalies but not renal. Studies on mRNA of XIAP (X-linked inhibitor of apoptosis protein) detected based on blood leucocytes PCR (polymerase chain reaction) showed that higher expression of XIAP mRNA is found in mosaicism and patients with renal malformations although not all the somatic features are explained by this anomaly. (10) The genetic diagnosis is essential in cases with short stature and dysmorphic disorders since mosaicism is seen in 10-20% of cases with Turner syndrome. (11) Chronic thyroiditis is constantly associated with Turner syndrome in a higher percent than general population with no specific pattern of karyotype correlations. (12, 13, 14)

The skeleton health is affected in monosomy but in cases with normal menses osteoporosis might not be seen. On the other hand the autoimmune gastrointestinal disorders as celiac disease contribute to vitamin D deficiency as seen here. (15) Others potential mechanisms are vitamin D receptor (VDR) gene polymorphisms as BsmI and FokI polymorphic sites of VDR in correlations to bone status in subjects with Turner syndrome. (16) Further studies found no correlation between thyroid disturbances and VDR polymorphisms (ApaI/G1025-49T, TaqI/T1056C, FokI/T2C and BsmI G1024+283A). (17) A higher bone turnover status was described in cases with Turner syndrome related hypogonadism and less probable if the menses are normal. (18) Overall the prognosis in Turner's syndrome variants is better than in classical variant since a small part of all classical complications are presented. On the other hand this is why the diagnosis might be delayed. (19,20)

Conclusion

The high index of suspicion in detecting a Turner syndrome variant is short stature despite the late diagnosis. The mosaic genetic line al-

lows the normal gonads and uterus development and thus a normal puberty timing and staging. The same karyotype background is correlated to discreet clinical changes as functional bicuspid aortic valves or small hearing defects.

Conflict of interest: none

Acknowledgement: we thank to the patient and her family for the consent; we also want to thank to the entire medical team involved in this case.

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