

A CASE OF MOSAIC TURNER'S SYNDROME

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INTRODUCTION

First described by Dr. Henry Turner in 1938,¹ Turner's syndrome also known as 45 X karyotype, Bonnevie-Ullrich syndrome, Monosomy X or XO syndrome is a chromosomal disorder affecting around one in 2500 female live births. It is characterized by gonadal dysgenesis, short stature and a variety of somatic anomalies. Many other organ systems are affected to varying degrees and at different stages of life. Turner's syndrome is not always accompanied by distinctive features and most often is not diagnosed in infancy. However later in childhood short stature may become obvious while in adulthood, the prominent features are those of sexual infantilism. One such case is reported.

CASE REPORT

A 19 year old unmarried girl was referred from department of paediatrics with the complaints of primary amenorrhoea and underdeveloped secondary sexual characteristics.

The patient had been under regular treatment of paediatricians and endocrinologist since the age of eight years due to stunted growth, her height being below the 3rd centile for her age (112 cms). At the age of 9 years, she was diagnosed as a case of Mosaic Turner's Syndrome on the basis of cytogenetic testing carried out at Armed Forces Institute of Pathology (AFIP), Rawalpindi. Her Growth Hormone (GH) assays (L-Dopa stimulation test and Triple stimulation test) at the age of 10 years were diagnostic of growth hormone deficiency. She was kept under observation and thoroughly investigated to rule out other causes of arrested growth and any co-morbidity. GH therapy in the form of 2 IU S/C, six days a week commenced at the age of 13 years. Her height at the commencement of GH therapy was 137 cm. Her height at 1st, 2nd and 3rd years of therapy was 140.5, 145.5 and 147.5 cms, respectively. She however failed to develop secondary sexual characteristics and to achieve menarche. She was put on conjugated estrogen (Tablet Premarin 0.625mg 1xOD) at the age of 17 years.

On examination the patient was found to be short statured with a short neck and having breast and pubic hair development at Marshall's and Tanner's stage 1.² Rest of the general physical and systemic examinations were unremarkable. Radiological examination revealed short 5th metacarpal. She was found to have elevated FSH and LH levels with decreased Estradiol levels suggestive of gonadal dysgenesis. Her ultrasound abdomen/pelvis revealed a hypoplastic uterus with absent ovaries as shown in Figure 1.

Anti-reticular and anti-gliaden antibodies were negative. Thyroid profile and cardiac imaging was normal. She was put on tablet Progyluton 1x OD (Estradiol valerate 2mg, Norgestrel 0.5mg) along with calcium supplements. She started having regular withdrawal bleeding and development of secondary sexual characteristics which were periodically examined on a three monthly basis. At present she stands 149 cms tall and weighs 58 kg with well-developed secondary sexual characteristics. She is performing well in academics and is presently studying in 1st year of computer sciences having secured 650 marks in matriculation examination.

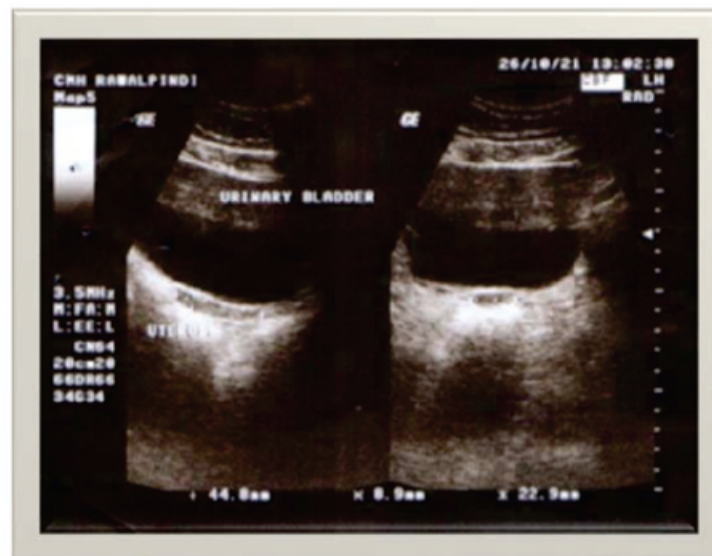


Fig 1. Hypoplastic Uterus with Non-visualized Ovaries

DISCUSSION

Turner's syndrome (gonadal dysgenesis) is an important cause of short stature in girls and primary amenorrhea in young women.³ It is characterized by the partial or complete absence of one X chromosome in some or all cells of the body (45X karyotype). A complete absence

in all cells is referred to as Classical Turner's Syndrome whereas occasionally, the X chromosome can be absent or abnormal in some, but not all of the cells of the body. This is described as "Mosaic Turner's Syndrome" which results in subtler symptoms.

Patients with Turner's syndrome are at risk of congenital heart defects (e.g. coarctation of aorta and bicuspid aortic valve) and may have progressive aortic root dilatation or dissection. There is also a risk of congenital lymphoedema, renal malformation, sensorineural hearing loss, osteoporosis, obesity, diabetes, autoimmune thyroiditis, inflammatory bowel disease and atherogenic lipid profile.³ Patients usually have normal intelligence but may have problems with non verbal, social, and psychomotor skills. Physical manifestations may be subtle but can include low set ears, a webbed neck, a broad chest with widely spaced nipples, a low posterior hair line, hypoplastic or hyperconvex nails, cubitus valgus, short 4th and 5th metacarpals and metatarsals, micrognathia and a high-arch palate. Turner's syndrome manifests itself differently in each female affected by the condition and no two individuals will share the same symptoms.³

Turner's syndrome occurs in one out of 2,500 to 3,000 live female births.⁴ Ninety-nine percent of conceptuses with a 45X karyotype abort spontaneously causing 10 percent of all first trimester miscarriages. Unlike Down's syndrome, maternal age does not increase the risk of Turner's syndrome and there are no clearly established risk factors. Recurrence in subsequent pregnancies is rare.⁴

The exact etiology is unclear although several theories have been proposed which implicate loss of crucial genetic complement usually expressed by both X chromosomes in females.

Diagnosis can be made in utero by chorionic villous sampling or amniocentesis on suspicion during antenatal screening based on ultrasound findings such as increased nuchal translucency, cystic hygroma, coarctation of the aorta, renal anomalies or polyhydramnios. None of these however, is diagnostic and karyotyping must be performed and repeated post-natally.⁵ Post-natal diagnosis should be considered in any girl with unexplained growth failure or pubertal delay. Elevated circulating FSH levels in girls in infancy or adolescence indicate gonadal failure and may point to Turner's syndrome. A diagnosis of Turner's syndrome can be easily missed as most of the features may be absent especially in mosaics.

Being a chromosomal disorder, there is no cure for the syndrome. However owing to the associated medical problems, a multi disciplinary approach is usually required for the management of these cases from diagnosis through to adult life.⁶ GH therapy should be considered in all girls with Turner's syndrome whose height is below the 95th centile for Turner's syndrome. GH accelerates growth, with earlier onset of treatment and higher doses

giving better outcomes. The usual dosage is from 4.7-9.3 mg/m²/week (0.16-0.32mg/kg/week), with most girls commencing on 0.23 mg/kg/week.⁷ Final height increments range from 5-15 cms with improvement in peak bone mass once given in combination with estrogen.

Over 90% of girls with Turner's syndrome have gonadal failure and require either pubertal induction and/or later maintenance estrogen therapy.⁸ Estrogen is essential for the physical changes of puberty including breast development, uterine and pelvic growth, and the psychological, social, emotional and sexual evolution of puberty. It is also essential for the achievement of peak bone mineralization. But, since estrogen also potently accelerates fusion of bony epiphyses, the timing of its commencement must be coordinated with GH therapy in order to achieve maximum growth potential, while not unduly delaying the onset of puberty. In general, estrogen should be given around age 12-13, but generally not later than age 14. Low dose estrogen therapy is commenced using a natural estrogen, preferably oestradiol valerate, 0.5-1mg on alternate days increasing the dose at 6-12 months interval with completion of feminization in 2-3 years. A progestin e.g. Medroxyprogesterone acetate, is added (5mg daily for 12-14 days each month) when vaginal spotting occurs or after 24 months of estrogen therapy in order to establish regular withdrawal bleeding. Transdermal estrogen patches may also be used.

Mental retardation is not a feature of Turner's syndrome yet owing to complex genetic and hormonal deficiencies, there is a multitude of psychological and body image issues such as limited emotional arousal, unassertiveness and over-compliance. Visio-spatial perception, mathematical ability and fine coordination may be affected and therefore appropriate psychological support should be offered.⁹

In Vitro Fertilization (IVF) and assisted pregnancy by oocyte or embryo donation is possible but due to the associated risk factors, a comprehensive medical, cardiac and gynaecological screening is imperative prior to any such procedure.¹⁰ Moreover preparation of the uterine lining may be required by optimal estrogen and progesterone therapy. Cephalo-pelvic disproportion may be an issue in some cases.

The presentation of Turner's syndrome can be highly variable, but short stature and infertility are almost always present. Surgical treatment may be required for CVS malformations. With appropriate medical management involving multiple specialties, the vast majority of patients are able to lead a normal life, attend mainstream school and have successful careers, relationships and family life.¹¹

REFERENCES

1. Turner, HH. A syndrome of infantilism, congenital webbed neck, and cubitus valgus. *Endocrinology* 1938; 28:566-74.
2. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. *Arch Dis Child* 1969; 44(235):291-303.
3. Saenger P. Turner's syndrome. *N Engl J Med* 1996; 335:1749-54.
4. Stochholm K, Juul S, Juel K, et al. Prevalence, incidence, diagnostic delay, and mortality in Turner syndrome. *J Clin Endocrinol Metab* 2006; 91:3897-3902.
5. Saenger P. Clinical review 48: The current status of diagnosis and therapeutic intervention in Turner's syndrome. *J Clin Endocrinol Metab* 1993; 77:297-301.
6. Bondy CA, Turner Syndrome Consensus Study Group. Care of girls and women with Turner syndrome: a guideline of the Turner Syndrome Study Group. *J Clin Endocrinol Metab* 2007; 92:10-25.
7. Ari M, Bakalov VK, Hill S, Bondy CA. The effects of growth hormone treatment on bone mineral density and body composition in girls with Turner syndrome. *J Clin Endocrinol Metab* 2006; 91:4302-4305.
8. Ross JL, Roeltgen D, Feuilleux P, et al. Use of estrogen in young girls with Turner syndrome: effects on memory. *Neurology* 2000; 54:164-170.
9. Rovet, JF. Behavioral manifestations of Turner syndrome in children: A unique phenotype. In: Turner syndrome in a life span perspective: research and clinical aspects, Albertson-Wikland, K, Ranke, MB (Eds), Elsevier, Amsterdam 1995; 285-97.
10. Bodri D, Vernaev V, Figueras F, et al. Oocyte donation in patients with Turner's syndrome: a successful technique but with an accompanying high risk of hypertensive disorders during pregnancy. *Hum Reprod* 2006; 21:829-32.
11. Ostberg JE, Conway GS. Adulthood in women with Turner syndrome. *Horm Res* 2003; 59:211-21.