

Nonmosaic 45, XO karyotype in a woman with Turner syndrome without any cognitive, psychosocial or behavioral deficiencies (A Case report)

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ABSTRACT

Enny S Pamuji, Djaswadi Dasuki : *Non 45 XO karyotype in a woman with Turner syndrome without any cognitive, psychosocial or behavioral deficiencies*

A 22 year old woman with primary amenorrhea came to The Reproductive Endocrinology and Infertility Centre, University of Gadjah Mada, Dr.Sardjito Hospital. She had no abnormalities in cognitive, psychosocial or behavioral capacities, she had almost completed her university degree. On examination she had no secondary sexual development, no pathognomonic abnormal phenotype related to abnormal karyotype. There was no indication of family history associated specifically to the abnormal karyotype, phenotype feature of Turner syndrome and a specific

The patient karyotype analysis of blood sampling indicated 45XO, and it failed to demonstrate any mosaicism. Laparoscopic examination revealed a hypoplastic-lobulated-unicorns uterus, as streak gonad at the left side and no ovary at the other side.

Keywords : Turner syndrome, non behavioral deficiencies, nonmosaic 45, XO karyotype, normal hormone level

ABSTRAK

Enny S Pamuji, Djaswadi Dasuki : *Non 45 XO karyotype pada seorang wanita dengan sindrom Turner tanpa kelainan kognitif, psikososial ataupun perilaku.*

Dilaporkan sebuah kasus sindrom Turner tanpa kelainan kognitif, psikomotorik maupun perilaku. Seorang wanita umur 22 tahun dengan amenorrhoe primer datang ke Pusat Reproduksi, Endokrinologi, dan Infertilitas Bagian Ilmu Kandungan dan Kebidanan Fakultas Kedokteran Universitas Gadjah Mada/ Rumah Sakit Pusat Dr.Sardjito, Yogyakarta. Dia tidak mengalami perkembangan seksual sekunder, tidak ada abnormalitas kognitif, psikomotorik maupun perilaku, dia hampir menyelesaikan pendidikan universitasnya. Pada pemeriksaan tidak ditemukan adanya kelainan yang berkaitan abnormalitas kariotipe. Analisis kromosom menunjukkan kariotipe 45XO, tidak ada *mosaicism*. Laparoskopi menemukan uterus unikornis-berlobula-hipoplastik, *streak gonad* tanpa ovarium pada satu sisi yang lain.

INTRODUCTION

Chromosome abnormality in Turner syndrome (TS) lies on the proximal part of the short arm of the X chromosome. They might be inherited or occur spontaneously, or occur in the environment in the utero life cycle¹. The most common TS (50%) occurs when a single X chromosome is lost yielding a monosomic condition with 45,XO. Thirty percent of individuals with TS have a mixed or mosaic condition. These individuals have some cells containing a normal 46, XX chromosome complement and other chromosomes that contain one or more abnormal chromosome complements, including the possibility of a 47, XXX karyotype. The most common mosaic condition is a 45,X/46,XX karyotype and a small proportion of individuals with mosaicism can have a 45,X/46,XY. The other 20 percent of individuals with TS have a structural abnormality in one of their two X chromosomes. This can reflect a ring X chromosome, an isochromosome or a deletion, rearrangement, or translocation of part of an X chromosome^{2,3}.

The chromosomal abnormalities causes ovarian failure in the early age before the puberty, spontaneous puberty occurs in 5-30% and the fertility rate varies from 5-10%. Otherwise, only 8-10% of non-mosaic Turner syndrome have normal ovarian function during puberty. Moreover about 50-55 % of the cases have deficiencies of the cognitive and physical performance. As adults, difficulties with relationship and coping with the TS condition are commonly reported. Due to their particular set of physical stigmata, females with TS generally have poor body image and low self esteem^{1,3}.

Three physical systems are affected in TS i.e. skeletal, reproductive and lymphatic systems. The most common physical defect in TS is short stature. Additional skeletal stigmata include a usual bend of carrying angle of the elbow and arms (cubitus valgus), a short forth-digit metacarpal, micrognathia, and a high arched palate, which can give rise to initial feeding and articulation difficulties and abnormality in orientation of the ear canal. The reproductive system defect involves ovarian dysgenesis and infertility. The lymphatic system defects are caused by abnormality in lymphatic clearance, which can give rise to the cystic brain

hygroma in utero, and permanent neck webbing in surviving neonates. Other common developmental defects include coarctation of the aorta, horseshoe kidneys, multiple pigmented nevi and nail dysplasia^{2,3}. The gold standard of diagnosis indicates abnormal karyotype with 45XO.

It will be reported an interesting case of TS syndrome with primary amenorrhoe, short stature but no other physical nor behavioral abnormalities.

CASE REPORT

The patient presented initially to us at the age of 22 years old with the chief complaint of primary amenorrhea. She appeared to be a phenotypic female. Childhood history was unremarkable except for short stature. For about 2 years ago she consulted with a gynecologist for amenorrhea complaint. Then, she took a medicine prescribed by the gynecologist, and menstruation for about 3 days that seemed to be like normal menstruation occurred. No increasing blood pressure history was found in this patient. There was no familial history with similar short stature or physical or mental development deficiency or primary amenorrhea. She has one sister with normal phenotypic appearance.

On physical examination, she presented normal mimics. She was 143 cm in height and 29 kg in weight. Her blood pressure was normal, 110/70 mmHg. Her breasts were small and undeveloped and were assessed to be at Tanner 1 stage. There was no pubic hair. Her external genitalia, major and minor labia, vaginal introitus, and shape and appearance were normal and the hymen was exist. On rectal examination, the length of the vaginal canal was found to be normal and the hypoplastic uterus was palpated. Using a transrectal USG, the uterus measured 3 cm in length, adnexa were free of masses and no distinct ovaries could be visualized. The measurement of hormone level revealed hypergonadotropin hypogonadism with an increase in the FSH level 86,16 mIU/ml, LH level 18,58 mIU/ml, whereas estradiol level was low that was 10,94 mIU/ml.

Non specific phenotype was also expressed with no sign of increasing carrying angles (cubitus valgus), a shield chest, a short forth-digit meta-

carpal, micrognathia and a high arched palate abnormalities, neck webbing, coarction of the aorta, horshoe kidney, multiple pigmented nevi and nail dysplasia. The only abnormalities were short stature and no sexual sex development such as no pubic or axillary hair, no breast bud development. The absence of this specific phenotype led to the late diagnosis and therapy for this patient.



FIGURE 1 – Patient physical appearance

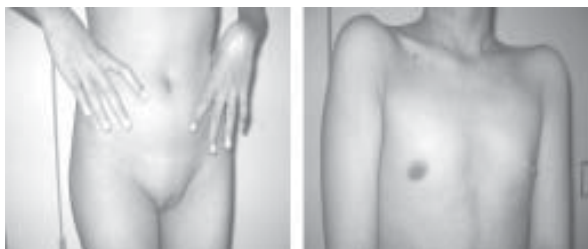


FIGURE 2 – Negattive pubic hair

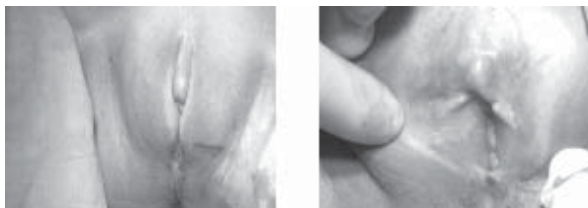


FIGURE 3 – No breast development

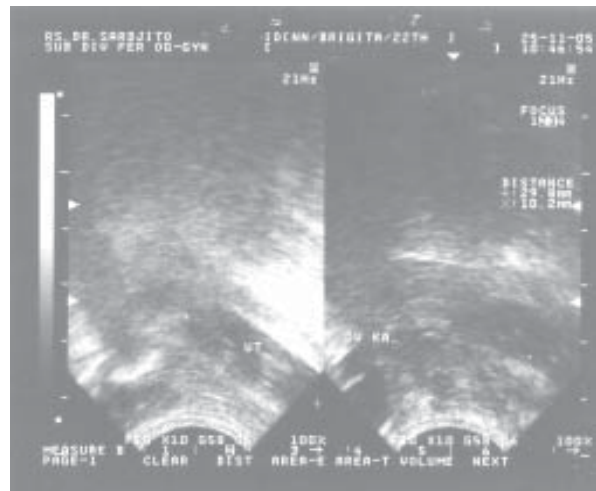


FIGURE 4 – Normal external genitalia

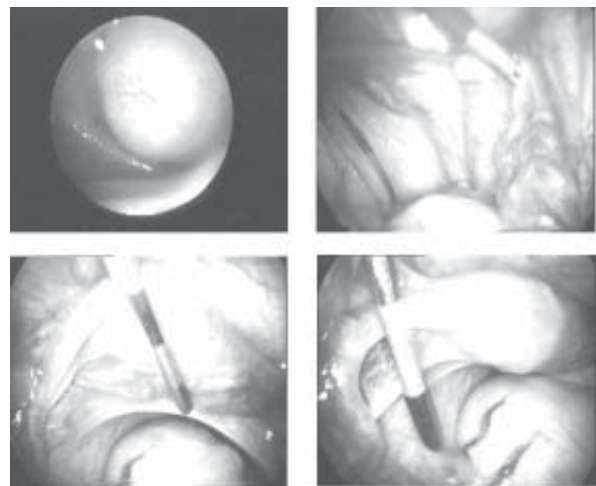
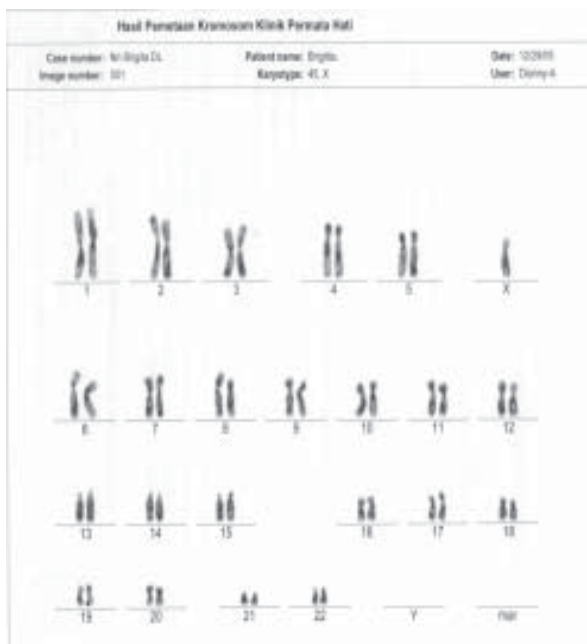


FIGURE 5 – Transrectal USG

A diagnostic laparoscopy was performed and found that there were an hypoplasia uterus, agenesis of right ovarian and disgenesis of left ovarian. The uterus was small in size (3x3x1 cm3), lobulated, unicornis. The right ovarian was absent and there was “streak gonad” on the left ovarian, with the size of 1x0, 5x0, 2 cm. We couldn’t find any testis in the pelvic cavity. Colposcopy using a hysteroscope revealed the vaginal canal was normal in length, for about 6 cm, and the cervix and an external uterine orifice were normal in shape and size.



Karyotype examination (the sample was taken from a peripheral lymphocyte) revealed a 45, XO with no mosaicism sign.

Chromosomal

The most interesting point in this case was there were no any deficiency in cognitive, psychomotor or behavioral capacities. She was a student in The Department of Language Science in the last semester at her age of 22 years old and this indicated that no cognitive deficit was found in this patient. There was no sign of behavioral abnormality as well, no history of anxiety, shyness, difficulty in understanding social clues.

The patient then got an estrogen replacement therapy orally once daily to prevent osteoporosis and to maintain normal female functioning.

DISCUSSION

Turner syndrome is the result of complete or partial X chromosome monosomy in a phenotypic female and associated with characteristics of clinical features. The most consistent characteristics are short stature and gonadal dysgenesis. The diagnosis is made on the basis of a chromosomal analysis. The diagnosis of TS may be delayed until adulthood in up to 10% women^{2,4}

The majority of women with TS will be infertile. Ovarian failure occurs within the first few months or years of life². Unless they receive estrogen replacement therapy during adolescent, females with TS remain sexually infantile throughout life. Pregnancy may be achieved through oocyte donation and in vitro fertilization^{5,6,7}. Pregnancy will increase the risk of cardiovascular complication, particularly aortic root dissection. Cardiological assessment is really needed before seeking to become pregnant. Hypertension must be monitored and treated aggressively^{8,9}

A significant number of females with Turner syndrome have deficits in specific area of intellectual performance. They usually have normal verbal ability but impaired nonverbal skill such as visual spatial processing, motor coordination, and perceptual abilities. The nonverbal impairment may be reflected by poor arithmetic skills, difficulty in constructional tasks, poor sense of direction, and difficulty in learning to drive. They may also have reduction in short term memory and attention span²

The severity of the cognitive impairment has been shown to be related to the karyotype. Murphy and colleagues demonstrated that female with 45, XO monosomy had significantly lower performance scores compared to females with mosaic karyotype. Those with mosaics were relatively unaffected compared to those with 45, XO karyotype in increasing number of social problem. Neurocognitive and social skill difficulties were found in women with Turner syndrome^{2,10}

A significant number of women with TS may complete a university degree, and the majority of TS women have little difficulty in finding employment. In long term, fewer than 5% people with TS achieve higher professional such as holding PhDs or becoming physicians or lawyers. Most adults minimally hold clerical or semiprofessional position (e.g. teaching, nursing, early childhood education). Compared to their siblings, the women with TS attain a similar educational level but are significantly lower in occupational level^{2,3}

There is a strong difficulty in processing numerical and mathematical information; many (but not all) individuals typically score very low on test of arithmetic achievement. The lack of X-chromosome material influences brain development

to yield abnormalities in the cerebral hemisphere that are greater on the right side than on the left. Girls with TS demonstrate particularly weak math processing abilities and are at high risk of nonverbal learning disability. Women with TS show specific cognitive deficits in visuospatial processing as well as in selective aspect of attention, executive processing and memory functioning. Specific neurophysiologic deficit that may affect adaptation includes four interacting areas of functioning: visual spatial deficit (e.g. difficulty in driving), defect in social cognitive (e.g. failure to appreciate subtle social clues), problem with nonverbal solving (e.g. mathematics) and psychomotor deficit (e.g. clumsiness)³

Women with TS tend to have characteristic personality traits. They find it more difficult to make friends and enter into sexual relationship. This may be due, in part, to difficulty in understanding nonverbal communication but also can be due to poor self-image as a result of short stature and delayed sexual maturation. As adult, many individuals with TS demonstrate a high degree of dependency and typically live at home with parents, although some of them do marry and have (adopted) families^{2,3}

One study reported that interindividual variation of intellectual abilities in Turner syndrome seems to be primarily related to familial coinfluences and not to the interindividual varying loss of X-chromosome DNA in terms of hidden mosaicism or potential associated risk factors such as the loss in terms of haploinsufficiency for a specific gene(s) on their distal part of the short arm of the X, a role of wide variation in (hidden) mosaic status, early deficiency of the sex corticosteroid in terms of hypergonadotrophic hypogonadism, which is caused by ovarian failure, and otitis media associated with hearing impairment¹¹

Age at diagnosis can vary in accordance with the phenotypic expressivity over the life span. The woman in this case didn't have any specific phenotypic expressivity, proven by normal cognitive, psychosocial or behavioral, except primary amenorrhea later in life. She could reach university degree at language science. From literature it is said that about 33% of adults TS went to university and 10% achieved postgraduate degree. Only about

63% of women with TS were ever married². Nonspecific phenotype was also expressed with no sign of (cubitus valgus), a short fourth-digit metacarpal, micrognathia and a high arched palate abnormalities, neck webbing, coarctations of the aorta, horseshoe kidney, multiple pigmented nevi and nail dysplasia, except the appearance of short stature and no sexual sex development such as no pubic or axillary hair, no breast bud development. The absence of this specific phenotype leads to the late of the diagnosis and therapy applied to this patient. There were also no signs of behavioral abnormality and no history of anxiety, shyness, and difficulty in understanding social.

CONCLUSION

A case of non mosaic Turner syndrome patient with no abnormalities in the cognitive, psychosocial or behavioral capacities has been reported. The woman in this case didn't have a specific phenotypic expressivity, proven by normal cognitive, psychosocial or behavioral, except if there is primary amenorrhea later in life. Analysis of Turner syndrome karyotype indicates non-mosaicism 45XO. From a diagnostic laparoscopy we found that there were a uterus hypoplasia, agenesis of right ovarian and dysgenesis of left ovarian. An estrogen replacement therapy administered orally one daily could prevent osteoporosis and maintain normal female functioning.

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