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Case Report

45,X/47,XXX KARYOTYPE AND FIVE PREGNANCY: ONE FIFTH SUCCESSFUL

45,X/47,XXX ve beş gebelik: Beşte bir başarı

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ABSTRACT

Mosaic karyotype, a relatively common phenomenon in Turner syndrome, effects the phenotype and clinical outcome. The majority of women with Turner syndrome are infertile. Even though pubertal development is possible in less than 10% of cases, spontaneous pregnancy frequency is 2%, and repeated gestation is even rarer. These conditions are usually observed in mosaic Turner patients. 47,XXX mosaicism is rare. In literature, pregnancy outcome in cases with 45,X/47,XXX karyotype is more successful than other Turner syndrome cases. We present a mosaic case for 47,XXX cell line who had one successful spontaneous pregnancy, and four miscarriages, due to the rarity of this condition.

Key Words: Mosaic Turner syndrome, 45,X/47,XXX, pregnancy

ÖZET

Turner sendromunun nispeten yaygın bir fenomeni olan mozaik karyotip fenotipe ve klinik sonuçlara etki eder. Turner sendromunda kadınların çoğu infertildir. Olguların %10'undan azında ergenlik gelişimi mümkün olmakla birlikte spontan gebelik sıklığı %2 olup tekrarlayan gebelik çok daha nadirdir. Bu durumlar mozaik Turner hastalarında daha sık görülür. 47, XXX mozaisizmi nadir görülür. Literatürde 45,X/47,XXX karyotip olgularında gebelik gelişiminin diğer Turner olgularına göre daha fazla görüldüğü bildirilmektedir. Biz bu makalede 47,XXX mozaik hücre hattına sahip bir olgunun başarılı bir spontan gebelikle birlikte 4 düşük geçirmesini, nadir karşılaşın bir durum olması nedeniyle sunduk.

INTRODUCTION

Turner syndrome is defined as a loss or structural abnormality of the second X-chromosome. It affects about 1:2500 live female births. Although the clinical features of Turner syndrome are heterogeneous, the most common ones are short stature and gonadal dysgenesis (1). Short stature is present in all patients. The onset age of ovarian failure depends on the chromosomal abnormality (2). Although about 50% of the cases have classical karyotype 45, X, another half of them has various chromosomal abnormalities containing karyotypes with an X-isochromosome or ring X, or mosaicisms. Around 3–4% of cases are mosaic for 47, XXX cell line (1,3,4). Natural fertility is a rare condition in Turner syndrome, and repeated gestation is even rarer (5, 6). Spontaneous pregnancies mostly arise in mosaic cases (7). According to the literature, the patients with 45, X/47,XXX karyotype have usually successful pregnancy (8). We present here a patient with mosaic Turner syndrome who had one successful spontaneous pregnancy, and four miscarriages, due to the rarity of this condition.

CASE REPORT

We present here 27-year-old woman with Turner syndrome who had five spontaneous pregnancies, four of which ended in abortion. Conventional cytogenetic analysis showed a 45,X[45]/47,XXX[5] karyotype. She demonstrated normal breast development and normal puberty. Menarche had happened at the age of 13 years, and her menstrual cycles had continued regularly. Her weight was 57 kg, and length 145 cm (BMI: 27.1 kg/m2). At the physical examination she had cubitus valgus, several cutaneous nevi on her arms in addition to the short stature. However she didn't have web neck, low hair line, and short fourth metacarpals. She graduated from primary school. According to the testimony of herself, her school performance was not good. Moreover she informed us that she had been operated on due to congenital hydronephrosis during childhood period.

Regarding laboratory investigations when she was 27.5-year-old: FSH 3.83 mUI/ml (3.5-12.5); LH 6.69 mUI/ml (2.4-12.6); and estradiol 105.6 pg/ml (12.5-166).

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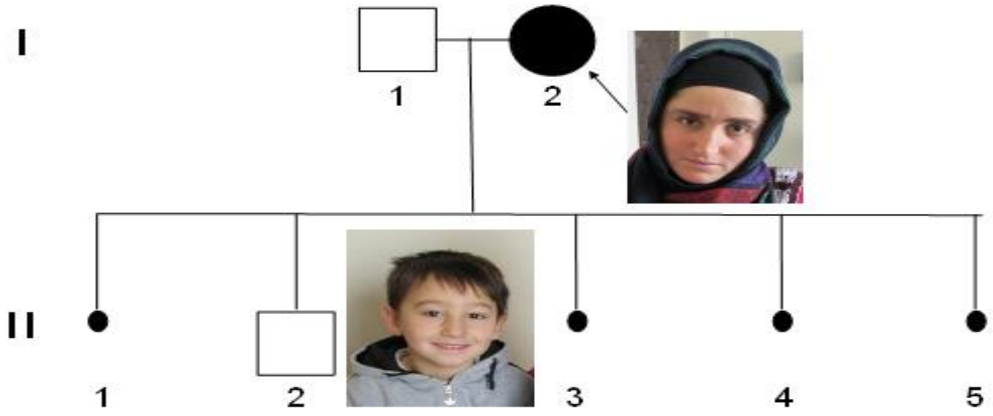

Figure 1. Pedigree of the family, and photos of the proposita and her son (Informed consent was obtained from patients).

Her thrombophilia panel containing factor V Leiden, prothrombin G20210A, methylenetetrahydrofolate reductase (MTHFR) A1298C, plasminogen activator inhibitor, and factor XIII mutations was normal, exclude MTHFR C677T heterozygous mutation. Thyroid function tests, and values for hemogram and biochemical patterns, urinalysis were also normal. Bone densitometry showed normal bone mineral density (Z-score: -0.4 SD). Audiometry didn't reveal any hearing loss. Cardiac echocardiography, pelvic ultrasonography did not determine any pathology. Renal ultrasonography demonstrated the bifid renal pelvis in the right kidney in addition to the lack of the left kidney.

Concerning the obstetric history, she experienced five spontaneous pregnancies, at the age of 21, 22, 26, 26 and 27 years, respectively. Recurrent miscarriages, while all was in 1.5 months, were reported (Figure 1). Her second pregnancy was successful and uncomplicated. She gave birth to a healthy boy when she was 22-year-old. Her baby was born via caesarean section due to cefalo-pelvic disproportion at 39th gestational weeks. Birthweight was 3370 gr (75th percentile), birth length and occipito-frontal circumference were unrecorded. Growth was normal and development milestones were achieved at timely fashion. He was examined at the age of 4-year 9-months. His weight was 20 kg (75th percentile), and height 113 cm (75th percentile), and he didn't have any dysmorphic feature (Figure 1). Conventional cytogenetic analysis showed a 46, XY karyotype.

DISCUSSION

The majority of women with Turner syndrome have gonadal dysgenesis, thus premature ovarian failure evolves. Spontaneous pubertal development, and spontaneous menarche, less often, may occur. As for spontaneous pregnancy, it is extremely rare condition, occurring in about 2% of the patients (2, 4). These situations arise mostly in the mosaic cases for 46,XX and/or 47,XXX cell lines, which shows that presence of the second X-chromosome is basic (7, 9). In fact 45,X/47,XXX karyotype has been reported as positive prognostic factor for spontaneous puberty in addition to normal sex steroids and gonadotrophins serum concentration (7). Our case had also all of these prognostic factors.

There is a high risk of fetal loss, congenital and chromosomal abnormalities, prematurity, and intrauterine growth retardation in the offspring of Turner syndrome (1, 2, 6). Present patient's son was healthy. Although the cases with 45,X/47,XXX karyotype described in the literature have usually had successful pregnancy rates and healthy children, this karyotype doesn't decrease the risk for congenital anomalies in the offspring (6, 9). In our case, four of the five pregnancies have resulted in miscarriage as well.

In addition to short stature and gonadal dysgenesis, cardiovascular, renal, skeletal anomalies, hearing loss, lymphedema, thyroid and gastrointestinal involvement may be seen in Turner syndrome. Moreover the learning disabilities may occur (1, 4, 7). Therefore women with Turner syndrome are also faced with serious complications associated with these problems during pregnancy. Hypertension, aortic dissection or rupture may appear as cardiac complication, gestational diabetes mellitus, thyroid disorders as endocrine complication. Besides the patients usually give birth via caesarean, owing to their pelvic structures are small (2, 7).

By reason of all mentioned maternal-fetal risks, women with Turner syndrome should be carefully followed in the course of their pregnancies. In our case caesarean section was indicated for cephalopelvic

disproportion. On the other hand, she didn't have any complication during gestational period.

Despite the fact that proposita has distinct short stature, and the history of congenital renal disease, the 45,X/47,XXX mosaicism diagnosis was not made until referring to the medical genetics outpatient clinics due to her recurrent pregnancy losses. The presences of normal sexual development, regular menstrual cycles, and spontaneous pregnancies have caused the delay in the diagnosis.

In summary, spontaneous pregnancy is possible even if it is very rare in Turner syndrome. Repeated pregnancies are even rarer, and carry serious risks for both patient and her offspring. These pregnancies mostly occur in women with mosaic karyotype. In these cases the constant manifestation is significant short stature. So we suggest that the clinicians should bring to mind the diagnosis of the mosaic Turner syndrome in women with significantly short stature especially in those with recurrent fetal loss and/or premature ovarian failure.

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