Spontaneous pregnancy and birth of a normal female from a woman with Turner syndrome and elevated gonadotropins

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Objective: To provide data for pregnancies in girls with Turner syndrome. Only 5%–10% of TS girls undergo spontaneous puberty and have menses. Spontaneous pregnancy occurs in 2%–7% of TS girls and is associated with a high rate of miscarriages, stillbirths, malformations, and chromosomal aberrations. Besides fetal problems, pregnancy in TS girls is of high risk for the mothers as well.
Design: Case report.
Setting: Academic unit.
Patient(s): One patient, now aged 28 years, was referred for short stature at age 13 years after an operation for coarctation of the aorta. The karyotype was 88% 45X, 5% 46XX, 5% 47XXX, 2% XO+Fr. The gonadotropin values at presentation and on follow-up ranged from high normal to high levels. Pubertal development and menses occurred spontaneously. At the age of 20 and 21 years, dominant follicles of 14 and 17 mm, respectively, were found on sonography. She conceived spontaneously at the age of 26 years and had an uneventful pregnancy, giving birth to a normal girl with normal chromosome constitution and birth weight of 2,800 g.
Intervention(s): None.
Main Outcome Measure(s): Pregnancy outcome.
Result(s): Successful spontaneous pregnancy.
Conclusion(s): Bearing in mind the serious problems of fertility and pregnancy outcome encountered in TS girls, we considered such a rare escape from the expected course of biological events to be worth reporting. (Fertil Steril® 2005;83:769–72. ©2005 by American Society for Reproductive Medicine.)

Key Words: Turner syndrome, pregnancy, karyotype, gonadotropins, ovulation, dominant follicle

Turner syndrome (TS) occurs in 1 in 2,500 female newborns. In about 50% of the cases, complete loss of one X chromosome is disclosed, whereas the rest of the TS patients display mosaicism or structural abnormalities of the X chromosome (1).

The phenotypic spectrum of TS is variable and includes any one of the following abnormalities in different combinations: cardiac defects (primarily coarctation of the aorta), kidney abnormalities, frequent ear infections, and anatomic stigmata like short or webbed neck. Short stature constitutes the most frequent finding, and it may be associated with minor anatomic stigmata (2). Increased incidence of thyroid disorders and especially Hashimoto's thyroiditis also has been reported in girls with TS (3).

With regard to ovarian dysfunction, TS is one of the principal causes of primary amenorrhea, caused by an accelerated loss of oocytes after the 18th gestational week or over the first postnatal months or years (4). The majority of TS patients have streak ovaries and partial or complete absence of secondary sexual characteristics. Consequently, infertility is one of the major problems that these women face at reproductive age (5). Nevertheless, spontaneous pregnancy occurs in 2% to 7% of girls with TS, but it is associated with a high rate of miscarriages, stillbirths, malformations, and chromosomal aberrations (6).

We report a woman with TS who conceived spontaneously and gave birth to a normal girl, along with a review of pertinent literature data and perspectives.

CASE REPORT

The patient, now aged 28 years, was initially referred to our hospital at age 13 years for short stature after an operation for coarctation of the aorta. At the initial examination, the height was 126 cm (SDS: −3.6), and she weighed 28 kg. She did not have the typical features of Turner's syndrome except for mild neck webbing. The breast development was stage III, according to Tanner criteria, and the pubic hair was stage I.

A GnRH test was performed, and basal FSH and LH values were 12 and 3.8 mIU/mL, respectively; no rise of either FSH (peak, 11.8 mIU/mL) or LH (peak, 4 mIU/mL) was observed. The external genitalia were normal. Ultra-

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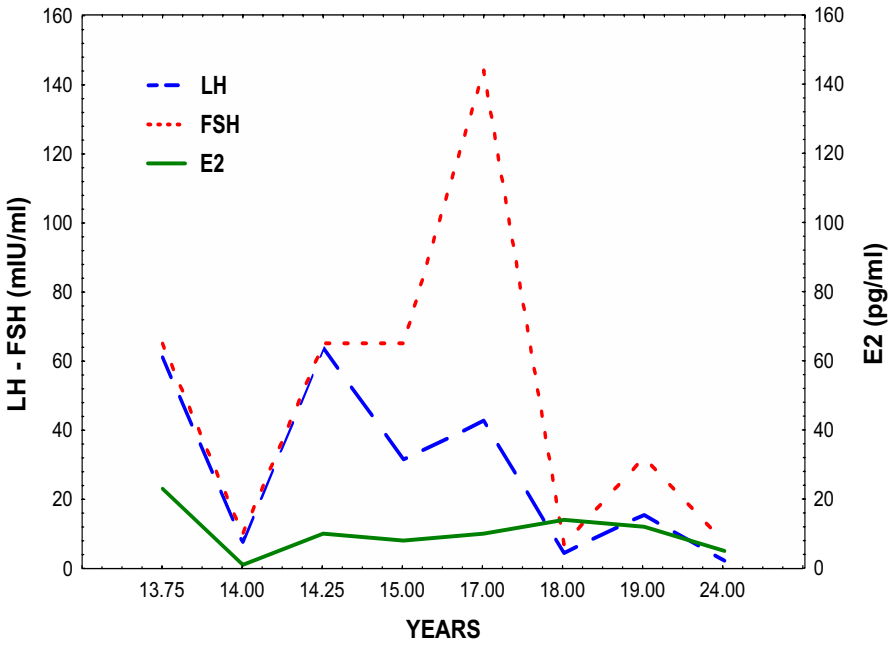
FIGURE 1

Values of gonadotropins and estradiol at various ages.



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sonography revealed a horseshoe kidney. Karyotype analysis showed 88% 45X, 5% 46XX, 5% 47XXX, and 2% XO+Fr. She received treatment with growth hormone for 2 years. Her final height is 152 cm (standard deviation score (SDS): −1.85). At the age of 14 years, hypothyroidism caused by Hashimoto's thyroiditis was documented, and thyroxine substitution therapy was initiated.

Her puberty progressed normally without estrogen therapy and menarche occurred at the age of 14 years. After the age of 16 years, her cycles were regular (menstrual cycle every 28 days; duration of menses, 4–5 days). LH and FSH values determined at different times ranged from high normal to very high levels (Fig. 1). At the ages of 20 and 21 years, dominant follicles with a diameter of 14 and 17 mm, respectively, were observed sonographically (Fig. 2).

At the age of 26 years, hypertension was detected, and the patient was started on antihypertensive medication. She married at age 26 years. She became pregnant spontaneously at 28 years, and treatment with antihypertensive agents was stopped. The pregnancy progressed uneventfully. Amniocentesis was carried out for karyotyping and showed a normal karyotype (46,XX). She delivered vaginally a normal female infant, weighing 2,800 g.

Institutional review board approval was not obtained for this study because all studies carried out and medications used were related to the patient's management requirements.

DISCUSSION

Ovarian function in patients with TS is variable; only 5%–15% of the girls have follicles at the time of puberty, undergo spontaneous pubertal development, and have menses. From one large series of patients with TS, it was shown that spontaneous puberty was positively correlated with the type of karyotype abnormality; spontaneous puberty was observed in 14% of 45,X0 patients and in 32% of patients carrying cell lines with more than one X (7).

It seems that the presence of the second X has a significant influence on the occurrence of spontaneous puberty. It is assumed that these patients possess the so-called critical region Xq13-q26, which contains genes that allow adequate ovarian development and function (8). A small percentage of patients with TS (2–7%) have spontaneous pregnancies (9). Karyotype structure is not decisive for spontaneous pregnancy, because pregnancies have been reported in patients with mosaics (as in our case) (10), with structural abnormalities (ring chromosome) (11), with 45,X (12, 13) and with 45,X /47,XXX mosaicism (14). The possible favorable effect of the presence of a small percentage of 46,XX and 47,XXX in our patient cannot be substantiated.

With regard to gonadotropin levels, it has been found that in TS girls with spontaneous puberty, gonadotropin levels are higher than those observed in normal girls who ovulate regularly but are lower than those observed in girls with streak ovaries (7). In our patient with spontaneous puberty and normal