Journal of Assisted Reproduction and Genetics, Vol. 21, No. 6, June 2004 (© 2004)

SHORT COMMUNICATION

GÖTEBORG, SWEDEN

Spontaneous Pregnancies in a Turner Syndrome Woman with Y-Chromosome Mosaicism

Submitted July 17, 2003; accepted April 29, 2004

***Purpose*:** To present a case involving pregnancies in a Turner woman with Y-chromosome mosaicism.
***Method*:** A descriptive case report of a single patient.
***Results*:** A 39-year-old woman was admitted to the endocrine clinic due to fatigue and premature menopause. She had tried in-vitro fertilization and oocyte donation twice without pregnancies but became spontaneously pregnant at age 36 and 37 and delivered two girls. During the seventh month of the second pregnancy, a dissecting aortic aneurysm, a coarctation, and subsequently a pheochromocytoma were detected and repaired. Hypothyroidism developed. Turner syndrome was diagnosed. Fluorescence in situ hybridization (FISH) analysis of lymphocytes revealed 31% XY cells and 4% XYY cells, while 66% of buccal cells had an XY constitution. Oophorectomy revealed no malignancy. FISH revealed 54% XY cells in the left gonad and 38% XY cells in the right.
***Conclusion*:** Turner syndrome should be suspected in women with aortic dissection, in general, but especially in those with additional features such as horseshoe kidney, coarctation, and infertility.

KEY WORDS: Aortic dissection; pregnancy; Turner syndrome; Y-chromosome.

INTRODUCTION

Turner syndrome (TS) is a chromosome aberration with the total or partial loss (mosaicism) of the second X-chromosome. The incidence is 1/2000 live born girls. TS is associated with hypogonadism, cardiac malformations, short stature, hearing problems, elevated liver enzymes, hypertension, hypothyroidism, and osteoporosis (1). Spontaneous puberty and spontaneous pregnancies are reported in some cases (2). The occurrence of a Y-fragment of the chromosome has been associated with an increased risk of gonadoblastoma, i.e. a potentially malignant gonadal tumor. Furthermore, cardiovascular disease and sudden death due to aortic dissection is a deleterious complication in TS (3,4). We report a case involving two spontaneous pregnancies at an advanced maternal age, aortic dissection during the second pregnancy, coarctation of the aorta, pheochromocytoma, premature menopause, and hypothyroidism. Furthermore, Y-chromosome mosaicism was present.

CASE REPORT

A 39-year-old nonsmoking, married woman was admitted to the endocrine outpatient clinic due to tiredness and premature menopause. She had had recurrent ear infections as a child and had a known horseshoe kidney. Menarche occurred at age 13. In-vitro fertilization was attempted twice at age 33. High stimulation was used with doses of 600 U follicle-stimulating/luteinization hormones (FSH/LH). This resulted in only one oocyte, which fertilized and embryo transfer was performed but did not lead to pregnancy. Two oocyte donation attempts were performed abroad without pregnancy. After that, at age 36, she became pregnant spontaneously and delivered a girl in 1997. Menstruation did not return, but she became pregnant again in 1998. Acute chest pain occurred during the seventh month of pregnancy and an examination revealed hypertension (160/110 mm Hg) and an aortic dissection. Another girl was delivered by acute Cesarian section, and the aortic dissection was repaired. The diameter of the aorta was 45 mm. A coarctation of the aorta was also noted and it was then corrected at a second operation later in 1999. The patient then experienced secondary amenorrhea with elevated FSH of 70 U/l.

She was just about to start work as a teacher again when she experienced sudden abdominal pain. An examination revealed gallstones and a 3-cm adrenal tumor. The catecholamines were 25 times above the upper reference level. A pheochromocytoma and the gall bladder were excised in 2000. Hypothyroidism was developing and she was admitted to the endocrine outpatient clinic. A physical examination revealed normal body composition, height 164 cm, blood pressure 125/80 mmHg, and no dysendocrine stigmata.

Turner syndrome was suspected. Free T4 was 12 pmol/l (reference level 10–22 pmol/l), thyroid stimulating hormone 2.9–8.0 mU/l (ref 0.2–4.0 mU/l), and thyroidperoxidase antibodies 7380 kU/l (ref < 100 kU/l). Thyroxine substitution was started.

1058-0468/04/0600-0229/0 © 2004 Springer Science+Business Media, Inc.

The karyotype of lymphocytes revealed 45,X in 30 mitoses. Due to an unusual gynecological history with two pregnancies above 30 years of age, Turner mosaicism was suspected. A fluorescence in situ hybridization (FISH) test was performed on buccal cells and lymphocytes. This revealed 66% XY in the buccal cells and 31% XY and 4% XYY in lymphocytes, respectively. The karyotype was 45,X[46]/46,X + mar[4] and an extended FISH analysis revealed an isodicentric Y-chromosome: ishidic(Y)(q11)(Ycen,Yp11.3)(DYZ3++, SRY++). The diagnosis was TS with mosaicism including an isodicentric Y-fragment. Both ovaries were resected in 2001 due to the known high risk of developing ovarian malignancy in the presence of a Y-fragment. Pathologic analysis failed to reveal any tumor. Hypoplastic ovaries with one corpora albicans without follicles were seen. FISH of the ovaries revealed 54% XY cells in the left gonad and 38% XY cells in the right gonad. Estrogen substitution was started. Bone measurement was normal.

DISCUSSION

Spontaneous pregnancies are rare (2%), especially after age 30 in TS (2). This is the first published case involving spontaneous pregnancy in a Turner woman with a Y-fragment. Furthermore, not only one but also two spontaneous pregnancies occurred at age 36 and 37. This new finding together with the known risk of gonadoblastoma in the ovaries in the presence of a Y-fragment (5) demonstrates the importance of FISH analysis as a complement to conventional karyotyping (6). Pheochromocytoma is not over-represented in TS.

Congenital heart defects, especially coarctation of the aorta and bicuspid aortic valves, are present in 17% of patients with TS, mainly in 45,X (7). Aortic dilation, dissection, and rupture are usually associated with an underlying factor such as coarctation, as in the case in this patient. There are rare cases in which there are no risk factors (3). The risk of acute aortic dissection was 6% in an American survey relating to TS and a review of the literature (3). The risk of mortality is high in such cases (3,4,8). A thorough cardiac and physical examination is warranted, particularly in the event of pregnancy (1,3,4,7,8). The pregnancy rate in TS has increased in recent years due to oocyte donation and in-vitro fertilization (8,9). The maternal risk of death from rupture of the aorta was 2% during pregnancy after oocyte donation in TS (8). Swedish Turner women have gone abroad for egg donation. Since 2003, this has also been permitted in Sweden.

This case demonstrates the importance of chromosomal analysis in the investigation of infertility and premature menopause. It also underlines the vital importance of a cardiac examination and an echocardiogram in known cases of TS before pregnancy, natural or assisted. TS should be suspected in women with an aortic dissection, in general, but especially in those with additional features such as horseshoe kidney, coarctation, and infertility.

REFERENCES

1. Saenger P, Albertsson Wikland K, Conway GS, Davenport M, Gravholt CH, Hintz R, Hovatta O, Hultcrantz M, Landin-Wilhelmsen K, Lin A, Lippe B, Pasquino AM, Ranke MB, Rosenfeld R, Silberbach M: Recommendations for the diagnosis and management of Turner syndrome. J Clin Endocrinol Metab 2001;86:3061–3069
2. Tarani L, Lampariello S, Raguso G, Colloridi F, Pucarelli I, Pasquino AM, Bruni LA: Pregnancy in patients with Turner's syndrome: Six new cases and review of literature. Gynecol Endocrinol 1998;12:83–87
3. Lin AE, Lippe B, Rosenfeld RG: Further delineation of aortic dilation, dissection, and rupture in patients with Turner syndrome. Pediatrics 1998;102:e12
4. Beauchesne LM, Connolly HM, Ammash NM, Warnes CA: Coarctation of the aorta: Outcome of pregnancy. J Am Coll Cardiol 2001;38:1728–1733
5. Hojbjerg Gravholt C, Fedder J, Weis Naeraa R, Muller J: Occurrence of gonadoblastoma in females with Turner syndrome and Y chromosome material: A population study. J Clin Endocrinol Metab 2000;85:3199–3202
6. Hanson L, Bryman I, Barrenäs M-L, Janson P-O, Wahlström J, Albertsson-Wikland K, Hanson C: Genetic analysis of mosaicism in 53 women with Turner syndrome. Hereditas 2001;134:153–159
7. Landin-Wilhelmsen K, Bryman I, Wilhelmsen L: Cardiac malformations and hypertension, but not metabolic risk factors, are common in Turner Syndrome. J Clin Endocrinol Metab 2001;86:4166–4170
8. Karnis MF, Zimon AE, Lalwani SI, Timmreck LS, Klipstein S, Reindollar RH: Risk of death in pregnancy achieved through oocyte donation in patients with Turner syndrome: A national survey. Fertil Steril 2003;80:498–501
9. Foudila T, Söderström-Anttila V, Hovatta O: Turner's syndrome and pregnancies after oocyte donation. Hum Reprod 1999;14:532–535

Kerstin Landin-Wilhelmsen,[1,3] Inger Bryman,[2] Charles Hanson,[2] and Lars Hanson[2]

[1]Endocrine Division, Sahlgrenska University Hospital, Göteborg, Sweden.
[2]Reproductive Medicine, Sahlgrenska University Hospital, Göteborg, Sweden.
[3]To whom correspondence should be addressed; e-mail: kerstin.landin@sahlgrenska.se.