Asian Pacific Journal of Reproduction

Journal homepage: www.apjr.net

Document heading doi:

Successful triplet pregnancy in an African with pure gonadal dysgenesis: A plus for assisted reproduction

Aziken M*, Osaikhuwuomwan J, Osemwenkha A, Iribhogbe O, Orhue A

Department of Obstetrics and Gynaecology, University of Benin Teaching Hospital, Benin-City, Edo state, Nigeria

ARTICLE INFO

Article history:
Received 5 October 2014
Received in revised form 10 February 2015
Accepted 15 February 2015
Available online 20 March 2015

Keywords:
Gonadal dysgenesis
Infertility
Assisted reproduction
Triplet pregnancy
Nigeria

ABSTRACT

Gonadal dysgenesis represents a congenital developmental disorder of the reproductive system, with its main gynaecologic manifestations being amenorrhea and infertility. We present a unique case of pure gonadal dysgenesis in an 'about to be' married lady resident in a society where high premium and success in marriage is dependent on childbirth. With astute evaluation and counseling, assisted reproductive technology (ART) was safely and successfully used in this case with eventual triplet pregnancy and delivery. Our index experience shows that situations with compromised fertility the availability and access to ART aids effective treatment planning and births a re-invigorated hope for family life.

1. Introduction

Gonadal dysgenesis describes congenital developmental disorder of the reproductive system characterized by a progressive loss of primordial germ cells on the developing gonads of an embryo[1]. This loss leads to extremely hypoplastic (underdeveloped) and dysfunctioning gonads mainly composed of afunctional fibrous tissue, hence the name streak gonads. The accompanying hormonal failure also prevents the development of secondary sex characteristics, resulting in a sexually infantile female appearance and infertility. While the phenotype is female without genital ambiguity the genotype may be either 45, XO (turner syndrome), 46, XX or 46, XY(pure gonadal dysgenesis) [2-4] .

Amenorrhea and infertility are the main gynaecologic challenge of the patients[3-5]. Successful pregnancies have been reported in cases of pure gonadal dysgenesis but such reports are few in low resource settings owing to the huge financial implication of assisted reproduction technology (ART)[6,7]. Moreso, with a high premium on child birth in Africa, young girls with such conditions in which fertility is abinitio compromised may ostracize themselves from a hope of family life. We present a case of pure gonadal dysgenesis in a young Nigerian who was counseled before marriage and eventually achieved successful pregnancy and delivery.

2. Case report

She was 32-year-old woman with a history of primary amenorrhea who presented with her fiancé with fertility concerns owing to amenorrhea. History revealed she had used hormonal drugs sparingly at some time to induce menses. On physical examination the breast was tanner stage 3, scanty axillary and pubic hair were observed, while the external genitalia were of normal female gender. An ultrasound revealed a small uterus (3.5 cm 3.0 cm 2.0 cm). Hormone assay showed elevated gonadotrophins: serum follicle-stimulating hormone (FSH) level was 52.20 mIU/mL, luteinizing hormone (LH) was 18.92 mIU/mL, prolactin level was 9.24 ng/mL, total testosterone level was 0.63 ng/mL, and estrogen was 27 pg/mL. Chromosome analysis revealed a 46, XX karyotype.

The patient was counseled on the implications of pure gonadal

*Corresponding author: YAziken Michael E., Department of Obstetrics and Gynaecology, University of Benin Teaching Hospital, Benin-City, Edo state, Nigeria.
E-mail: michaelaziken@hotmail.com

dysgenesis viz menstruation and fertility and the option of ART using donor oocytes to circumvent fertility challenge. She was further encouraged to disclose findings and treatment options to the fiancé before marriage, this she did and they both agreed to follow through with treatment. She was commenced on estrogen hormone replacement therapy (HRT), with each HRT cycle resulting in menstruation and better development of secondary sex characteristics. Semen analysis on husband's spermatozoa was normal.

Shortly after marriage, the couple came in for in-vitro fertilization (IVF) using donor oocyte as earlier counseled. She had 2 failed IVF cycles using donor oocyte between 2009 and 2011. In 2012 she had a third attempt with day 2 transfer of 4 embryos at 4 cell stage. Fourteen days after transfer, β-HCG of peripheral blood (pregnancy test) was positive and 4 weeks post transfer, pregnancy was confirmed with demonstration on transvaginal ultrasound of 3 gestational sacs with active fetal nodes. She continued hormonal support with estrogen and progesterone. At 10 weeks she had cervical cerclage inserted with no complications. Pregnancy remained uneventful until at 26 weeks and 4 days gestation when she was observed to be having preterm contractions and cervix dilated with membranes intact but bulging, a bed side ultrasound showed that fetuses were alive, there was no fever and full blood count, malaria parasite and urine culture results were all normal. She was admitted and nursed in an head-down tilt, cerclage was removed and tocolysis was commenced using salbutamol while she had a course of steroid (dexamethasone), the neonatologist were informed. The contractions abated after 24 hours and she was observed on admission. On the ninth day on admission at 27 weeks and 6 days her blood pressure was elevated 150/90 mmHg and this worsened the following day with observation of proteinuria, a diagnosis of severe preeclampsia at 28 weeks was made and patient was counseled for an emergency caesarean section. Three healthy babies were born; male 1.17 kg (apgar score(AS) 4 in 1 and 6 in 5), female 1.26 kg (AS 6 in1 and 8 in 5) and male 0.95 kg (AS 6 in1 and 8 in 5). They were successfully managed in the neonatal intensive unit and discharged home after 8 weeks with weight of 2.01 kg, 1.82 kg and 1.70 kg respectively. They were seen at 6-months follow up and found to be physically and mentally healthy.

3. Discussion

This case represents a classic 46, XX pure gonadal dysgenesis syndrome. Although the underlying etiology remains unknown in most cases, several genes have been implicated including mutation of SRY gene. The SRY gene is responsible for initiating male sexual differentiation, and mutation or deletion of SRY would induce the failure of the indifferent gonad to develop into a testis[5,8]. Researchers have described gonadal dysgenesis with female phenotype as the absence or insufficient development of the ovaries with consequent primary amenorrhea and variable hypogonadism or impuberism, depending on the degree of gonadal development. The karyotype can be 46, XX; 45, X0; 46, XY or mosa¨ıcism 45, X/46, XX; 45, X/46, X, del(X)(p22.2); 46, X, i(Xq) [1,2,8].

Primary amenorrhea, underdevelopment of mammary glands and lack or poor development of pubic hair as seen in this patient are the main presenting complaints. Also the patients with gonadal dysgenesis 46XX have lowered levels of estrogens and elevated levels of FSH and LH[5,6]. Diagnosis of pure gonadal dysgenesis 46XX was confirmed in this case on chromosomal analysis. Surgical removal of the gonadal streaks is necessary to avoid the possibility of neoplasia.[5,9,10]. However, this patient did not require this as she was 46 XX karyotype and as such not predisposed to malignant transformation.

Pregnancies have been reported before in cases of gonadal dysgenesis[5,6,9,10]; however, such occurrence remains strange in our setting. The positive response of this patient in terms of secondary sexual characteristics and reproductive tract changes to hormonal replacement therapy cycle further buttresses observations that 46, XX or XY pure gonadal dysgenesis patients could be able to accommodate successive pregnancies after hormonal replacement therapy for certain period[11].

This case represents a unique situation of latent infertility in a single Nigerian lady resident in a place where high premium and success in marriage is dependent on childbirth[12]. The availability of ART services in a public institution like ours helped in treatment counseling and consolidation of the patients' hopes[13]. Previous reports advocates early discovery of such condition in the pubertal period, so that both physical and mental therapies can be instituted as early as possible to enhance good outcome[4,5]. Although this patient presented late, in-depth exposition of the condition and psychological counseling with prospects of treatment from available ART services aided disclosure to her partner. Consequently her partner's awareness and support encouraged the resolve and determination to see through several IVF cycles until she achieved success. She had prophylactic cerclage because it was triplet gestation; Prophylactic cerclage has been shown to decrease significantly the incidence of preterm and extremely LBW neonates in triplet pregnancies[14]. Despite having an inevitable preterm delivery the premium care accorded by the neonatal unit of the hospital ensured good outcome. Preterm delivery have been previously observed, suggesting possible alteration in the functional capacity of the uterus in cases of gonadal dysgenesis[10,15]. However other researchers have hypothesized that in patients with gonadal dysgenesis the hypoplastic uteri, although able to be hormonally stimulated to accommodate a pregnancy, may

lack the receptors or the anatomical ability to dilate appropriately in labour, leading to a higher Caesarean section rate amongst this group[16,17].

In conclusion, education and effective communication of the prognosis and treatment options in conditions such as gonadal dysgenesis with seemingly compromised fertility can birth a dogged determination, support and perseverance by all concerned to achieve desired results. With astute evaluation and counseling, assisted reproductive technology can be safely used in females with chromosome abnormalities and gonadal dysgenesis.

Declare of interest statement

We declare that we have no conflict of interest.

References

[1] Berkovitz GD, Fechner PY, Zacur HW, Rock JA, Snyder HM, Migeon CJ, et al. Clinical and pathologic spectrum of 46,XY gonadal dysgenesis: its relevance to the understanding of sex differentiation. *Medicine* 1991; **70:** 375-383.

[2] Kristiina Aittomaki. The genetics of XX gonadal dysgenesis. *Am J Hum Genet* 1994; **54:** 844-851.

[3] Gorgojo JJ, Almod´ovar F, L´opez E, Donnay S. Gonadal agenesis 46, XX associated with the atypical form of Rokitansky syndrome. *Fertil & Steril* 2002; **77**(1): 185-187.

[4] Marrakchi A, Belhaj L, Boussouf H, Chraibi A, Kadiri A. Pure gonadal dysgenesis XX and XY: observations in fifteen patients. *Ann Endocrinol (Paris)* 2005; **66**(6): 553-556.

[5] Baron J, Warenik-Szymankiewicz A, Miedzianowski J, Baron JJ. New aspects of diagnosing and treating pure gonadal dysgenesis 46XY and 46XX. *Endokrynol Pol* 1993; **44**(4): 483-496.

[6] Cornet D, Alvarez S, Antoine JM, Tibi C, Mandelbaum J, Plachot M, et al. Pregnancies following ovum donation in gonadal dysgenesis. *Hum Reprod* 1990; **5:** 291-293.

[7] Plante BJ, Fritz MA. A case report of successful pregnancy in a patient with pure 46, XY gonadal dysgenesis. Fertil Steril 2008; 90: 2015.e1-2.

[8] Sánchez-Moreno I, Canto P, Munguía P, de León MB, Cisneros B, Vilchis F, et al. DNA binding activity studies and computational approach of mutant SRY in patients with 46, XY complete pure gonadal dysgenesis. *Mol Cell Endocrinol* 2009; **299:** 212-218.

[9] Chen MJ, Yang JH, Mao TL, Ho HN, Yang YS. Successful pregnancy in a gonadectomized woman with 46,XY gonadal dysgenesis and gonadoblastoma. *Fertil Steril* 2005; **84:** 217.

[10]Ko PC, Peng HH, Soong YK, Chang SD. Triplet pregnancy complicated with one hydatidiform mole and preeclampsia in a 46,XY female with gonadal dysgenesis. *Taiwan J Obstet Gynecol* 2007; **46:** 276-280.

[11]Kan AK, Abdalla HI, Oskarsson T. Two successful pregnancies in a 46,XY patient. *Hum Reprod* 1997; **12:** 1434-1435.

[12]Araoye MO. Epidemiology of infertility: social problems of the infertile couples. *West Afr J Med* 2003; **22**(2): 190-196.

[13]Orhue AA, Aziken ME, Osemwenkha AP, Ibadin KO, Odoma G. In vitro fertilization at a public hospital in Nigeria. *Int J Gynae Obstet* 2012; **118:** 56-60.

[14]Andrew Elimian, Reinaldo Figueroa, Sarvesh Nigam, Uma Verma, Nergesh Tejani, Nancy Kirshenbaum. Perinatal outcome of triplet gestation: Does prophylactic cerclage make a difference? *J Matern–Fetal & Neo Med* 1999; **8**(3): 119-122.

[15]Chen CP, Hwu YM, Yeh LF, Chern SR, Lee CC, Wang W. Successful triplet pregnancy and delivery after oocyte donation in an infertile female with chromosome mosaicism for monosomy X, partial trisomy X, and terminal Xp deletion. *Fertil Steril* 2003; **79**(5): 1231-3.

[16]Kan AKS, Abdalla HI, Oskarsson T. Two successful pregnancies in a 46, XY patient. Hum Rep 1997; 12(7) : 1434-1435.

[17]Frydman R, Parneix I, Fries N. Pregnancy in 46 XY patient. *Fertil Steril* 1988; **50:** 813-814.