48 XXYY KARYOTYPE IN A FEMALE WITH RECURRENT PREGNANCY LOSS: A CASE REPORT

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Background

48 XXYY is a rare sex chromosome abnormality with an estimated incidence of 1 in 18,000-40,000 live male births, which typically presents in phenotypic males with features similar to Klinefelter syndrome (47, XXY) [1]. No literature is available regarding manifestations of 48, XXYY karyotype in females, however manifestations in other reported sex chromosome aneuploidies involving Y chromosome in phenotypic females include infertility, dysgenetic gonads, and increased risk of gonadoblastoma [2].

Objective

To present a case of 48, XXYY in a phenotypic female with intact SRY genes identified on routine karyotype and FISH during workup of recurrent pregnancy loss.

Materials and Methods

A 43-year-old G7P1061 female presented with history of secondary infertility in the setting of recurrent pregnancy loss. She had six prior early pregnancy losses between 5-9 weeks as well as one uncomplicated pregnancy with delivery of a healthy phenotypic female via cesarean section at term. All pregnancies were achieved with her current partner. She reported normal puberty and 28-day regular menstrual cycles since menarche at 11 years old. Her medical history included primary hypothyroidism secondary to Hashimoto's thyroiditis, well controlled on 75mcg levothyroxine daily, as well as Major Depressive Disorder for which she was on Bupropion 150mg and followed with psychiatry. On exam, patient had normal appearing female external genitalia, vagina and cervix, as well as a normal, anteverted uterus. Breast exam was within normal limits with normal nipple spacing. FSH, LH, estradiol, progesterone, prolactin, and TSH were all within normal limits. An antiphospholipid panel, Factor V Leiden and ANA were negative. AMH was 0.45 ng/mL and consistent with diminished ovarian reserve. A hysterosalpingogram revealed a uterus with an arcuate contour and two suspected fibroids as well as patent fallopian tubes of normal caliber. Chromosome analysis revealed abnormal sex chromosome complement, XXYY. An internal SRY FISH was performed and showed normal localization on both Y chromosomes excluding a large deletion of the SRY target region.

Results

The patient was referred to genetics and given history of multiple miscarriages and abnormal karyotype, plan was made to pursue in vitro fertilization with preimplantation genetic testing as well as genetic testing for her current living daughter. Donor oocytes were discussed as well.

Conclusion

Despite the presence of the Y chromosomes and normal SRY, this patient presents as phenotypically female with functioning gonads and ability to carry a full-term pregnancy, although with significant history of recurrent pregnancy loss. This suggests that expression of phenotypic sex in these patients may be due to the involvement of other sex-determining genes and transcription factors or pathways such as SF-1, SP1, WT1 and MPK signaling pathway.

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References:

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