Undiagnosed maternal Triple X Syndrome mosaicism as a contributing cause of IVF failure and long term infertility in a private practice setting in Lima-Peru. A case report

Gisela Valer Chavez, MD[1]. Ither Sandoval, MD[2] ;

1. Naprotecnologia y Fertilidad Natural Perú
2. President of the Peruvian Society of Obstetrics and Gynecology.

Background

. Restaurative reproductive medicine places the effort in evaluating and treating women with infertility to identify and treat the underlying causes in a couple-centered approach. IVF centers usually screen patients to receive treatments based on their age and antimullerian hormone (AMH) values, skipping over the root causes.

Triple X syndrome (47, XXX) is a sex chromosome aneuploidy in which females have an additional X chromosome, in contrast to 46, XX karyotype in typical females. Its incidence is 1 in 1000 female births, being the most common, but underdiagnosed sex chromosome disorder. The majority of girls with triple X syndrome remain undiagnosed until adulthood when the genetic defect is discovered for other reasons like infertility. Our patient was diagnosed as diminished ovarian reserve (DOR) and she received unsuccessful treatments using assisted reproductive technology (ART) for years, but following our medical perspective, we found out that she was a triple X mosaic female.

We present this case to highlight the importance of paternal karyotyping in patients with decreased levels of AMH and unexplained or partially explained infertility.

REFERENCES

. 1.-Rafique M, AlObaid S, Al-Jaroudi D. 47, XXX syndrome with infertility, premature ovarian insufficiency, and streak ovaries. Clin Case Rep. 2019 May 14;7(6):1238-1241.

2.-George S, Dagar V, Chakrabarty BK, Nagaraja N. Unravelling the Impact of an Additional Sex Chromosome in an Adult Female. J Hum Reprod Sci. 2023 Apr-Jun;16(2):166-169..

3.-Wyrwoll, Margot J., Rudnik-Schöneborn, Sabine and Tüttelmann, Frank. "Genetic counseling and diagnostic guidelines for couples with infertility and/or recurrent miscarriage" *Medizinische Genetik*, vol. 33, no. 1, 2021, pp. 3-12.

CASE PRESENTATION

A 41 y/o woman with infertility, the couple had been trying to conceive for 8 years. She reported a normal menarche at 10y/o and regular menses . She had normal height ,weight and intellectual and social behavior.
Medical history: Abortion 21 y/o same partner. 01 Intrauterine insemination and 02 IVF attempts without success. Physical exam, 1,58cm and 64 kg. Other findings unremarkable.

Laboratory: Antimullerian hormone: 0,23 ng/ml Vitamin D: 23.9 ng/ml.
Transvaginal ultrasound: Normal.

Intervention(s)
Medical record, laboratory findings, imaging studies , G-banding karyotype.

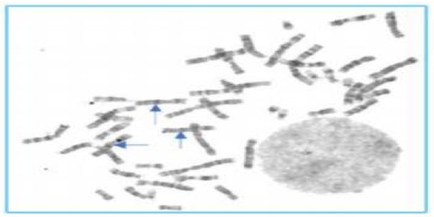
RESULTS:

A triple X chromosomal mosaicism 47, XXX[3] / 46, XX [47] was found in the cytogenetic studies

Genética
Instituto de Medicina Genética

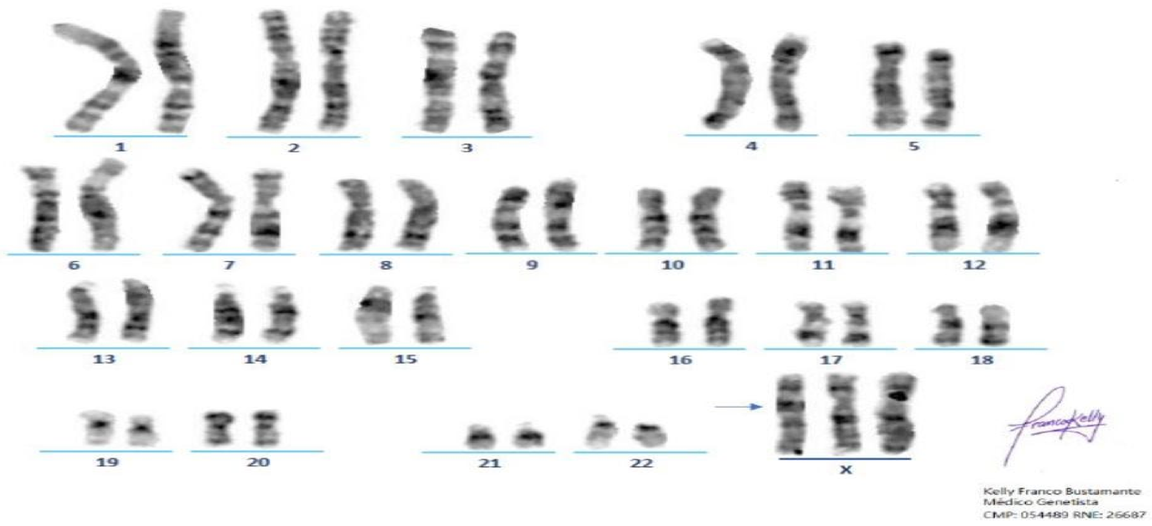
Estudio Citogenético

Código de muestra	:	SP23-063
Nombre	:	PARRA HUAROTO, ANA CECILIA
Tipo de Muestra	:	SANGRE PERIFERICA
Nro. de Células	:	3
Lámina	:	3P
Coordenadas	:	33,4/107,8
Hecho por	:	DB/FCH
Bandas	:	GTG



CARIOTIPO :

47,XXX



Kelly Franco Bustamante
Médico Genetista
CMP: 054489 RNE: 26687

DISCUSSION

It is considered that only 10% of individuals with trisomy X remain undiagnosed until adulthood when the genetic defect is discovered for other reasons like infertility. Patients presenting with developmental delay, hypotonia, learning disabilities, emotional or behavioral difficulties, or dysmorphic face are diagnosed earlier usually in childhood.
About 40 % of women with infertility have menstrual abnormalities that could reflect an ovarian dysfunction and a premature ovarian failure may develop over time. Karyotyping reveals a gonosomal aberration in 10–13 % of women with ovarian dysfunction, such as Turner syndrome or trisomy X (47, XXX). The knowledge of an abnormal karyotype is important for further management, since women with trisomy X have largely normal fertility but may develop premature ovarian failure(POI).

CONCLUSIONS

In patients with a very low AMH value, unexplained or partially explained infertility, parental karyotyping should be performed after individual assessment of the risk, in order to give an accurate diagnosis and prognosis, even in a phenotypically normal woman.
The so called “diminished ovarian reserve” based on the AMH values, does not explain infertility per se and we recommend a complete and expanded infertility work-up, considering a couple-centered approach, mainly in patients with long-term infertility.