Novel unbalanced X-A Translocation in an adolescent with Primary Ovarian Insufficiency

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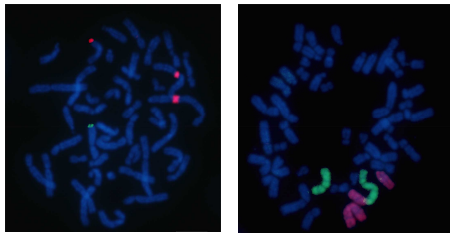
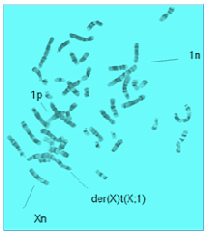
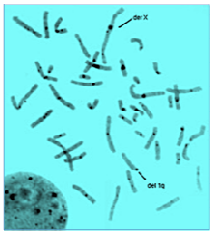
Translocations X-A usually produce alterations in the gonadal development of both sexes.
The participation of the X chromosome in the premature ovarian failure (POF),
expression more severe of the diminished ovaric reserve (DOR),
has been documented by different balanced and unbalanced X-A translocations,
to involve critical areas for the normal ovarian development in Xq.

The purpose is to document as a combination of classical and molecular cytogenetic studies allowed us to detect a novel non reciprocal translocation in a young woman with hypergonadotropic ovarian failure.

Patient of 14 years without the somatic stigmata of Turner syndrome.
Consulted for the first time at the 3.1 yrs by short stature (below Pc3).
During its infancy she presented a poor growth (Pc 3-10).
She had at age 11 a spontaneous breast development.
Currently she is 14 yrs. but she has not yet had the menarche.
The pelvic ultrasound showed a normal uterus and both ovaries, being 4cc the volume of the right ovary and 1,8 cc the left ovary.
The hormonal levels of FSH, LH, Estradiol and AMH were: 122.9 mUI/ml, 67 mUI/ml, Estradiol < 10pg/ml and 5,4 pmol/m, respectively.
The BMD lumbar Z score: -198 SDS.



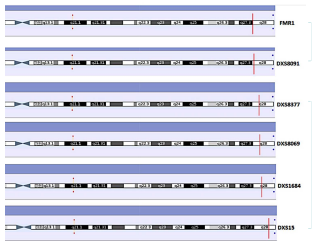


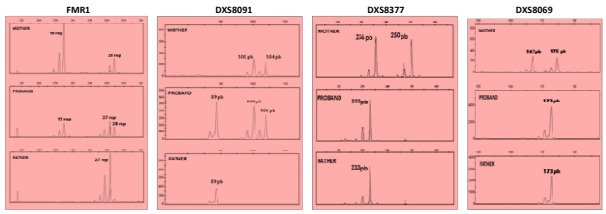


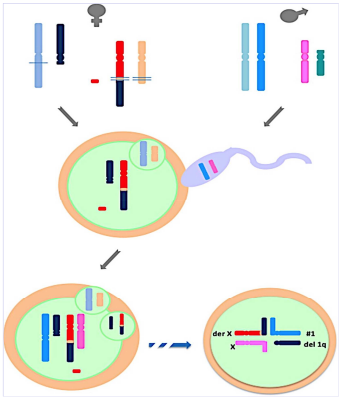
Classical and molecular cytogenetic studies in the proband and their parents:

- Chromosomal analysis with CTG, CBG and RHG banding techniques
- Replication patterns of X chromosomes with BrdU
- FISH with whole painting probes for chromosomes 1 and X
- FISH with constitutive heterochromatin 1q12 + Xq28 probes
- QF-PCR to determine the expansion of the triplete CGG of the FMR1 gene
- QF-PCR with the STRs DXS8091, DXS8377, DXS1068, DXS8069 and DXS15
- linked to Xq28 corresponding to the region of the POF1 gene

Patients	FMR1 Xq27.3 147,911,951-147,951,127	DXS8091 Xq28 148,521,335-148,521,437	DXS8377 Xq28 150,398,202-150,398,447	DXS8069 Xq28 150,468,886-150,469,049	DXS1686 Xq28 150,957,225-150,957,372	DXS15 Xq28 153,346,585-153,346,897
Proband	3 alleles: 19, 27 and 28 repeats	89/100/104	233	173	139	156
Mother	2 alleles: 19 and 28 repeats	100/104	236/250	167/175	129/139	156 / 160
Father	1 allele: 27 repeats	89	233	173	139	156







De novo X-A unbalanced translocation with interstitial dup(Xq27.3q28) and distal deletion Xq28.

POI could be caused by:

- haploinsufficiency of genes in Xq28 necessary for normal ovary develpment
- Asynapsis of the involved chromosomes during meiosis leading to apoptosis of germ cells in the ovary
- Duplication of FMR1 gene
- an epigenetic effect due to positioning within proximity of constitutive heterochromatin, resulting in silencing of genes in X-chromosome.