Newborn with a derivative chromosome X and ambiguous genitalia

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Translocations involving the short arms of the X and Y in human chromosomes are uncommon. One of the primary functions of the X and Y chromosomes is gender phenotype determination. Here we report a newborn female with ambiguous genitalia and abnormal X chromosome.

Karyotype was performed using the standard methods and Fluorescence in situ hybridization (FISH) directed for the SRY gene was used for confirmation of the clinical and cytogenetic suspicion. Chromosomal microarray analysis (CMA) was performed using CytoScan HD (Affimetrix®) to identified gains/loses on the der(X) chromosome.

The analysis revealed one abnormal X chromosome in a female karyotype. Considering the ambiguous genitalia clinical information the abnormal X was considered to be compatible with a translocation X/Y. This was confirmed by the presence of signal for the SRY using FISH.

CMA allowed to clarify a loss of 12.34 Mb at Xp22.33p22.2 and a gain of 7.41 Mb at Yp11.31p11.2 (ISCN = arr[GRCh37] Xp22.33p22.2(2703632_15050955)x1,Yp11.31p11.2(2650140_10059230)x1).

The X deleted region includes several OMIM morbid genes, including CLCN4. Mutations in CLCN4 are associated with intellectual disability and impaired language development, and heterozygous females can be as severely affected as male. The gain on the Y encompasses nine OMIM genes, including the SRY gene, involved in the sexual male development. This additional information can be of great value for the child development.

Translocations of segments of Y chromosome containing SRY are described in sexual reversion and true hermaphroditism cases, which could explain the reason for referral for the newborn.

Nevertheless, translocations between the X/Y chromosomes in females are expected to have a skewed inactivation pattern in favour of the abnormal X and X-inactivation studies could prove this likelihood. If a normal developmental of the child is observed over time this will be likely due to the preferable inactivation of the abnormal X.

Presently the child is about 1-year-old and she presents normal uterus, ovarian, and external genitalia, with absence of male gonads. No other clinical features have been identified.