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DNA analysis of sex chromosomal aberration: curious mutation found in Turner syndrome

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Abstract. The clear evidence that curious fashion of mitochondrial DNA (mtDNA) inheritance was reported in sex chromosomal aberration. Human mtDNA is located outside the nucleus of the cell producing energy for the cell. In the recent years, mtDNA is being used in forensic DNA identification because each cell has many copies of mitochondria, and is easy to be amplified by PCR. Human mtDNA has polymorphic sites in hypervariable regions (HVR) I, II and III. However, human mtDNA evokes some problems, such as heteroplasmic point mutations and questionable maternal inheritance. To investigate this phenomenon, we had a chance to perform a mtDNA testing on 1-month-old infant, diagnosed as Turner Syndrome which was confirmed to be 45XO karyotype by X-STR testing. As a result, two remarkable evidences were obtained. The first, an intermarriage, is seemed to be related in the genesis of the sex chromosomal aberration. The second, the exact maternal inheritance of mtDNA was not maintained in Turner syndrome, as well as in Klinefelter syndrome reported by us previously. In these cases, although paternal influence of mtDNA inheritance was deniable, mutations of mother's mtDNA were excluded or repaired to the usual type in child's mtDNA.

Keywords: Turner syndrome; MtDNA; Maternal inheritance; Mutation; X-STR

1. Introduction

In 1938, Turner presented a syndrome composed of a variety of congenital anomalies such as small stature, delayed sexual maturity, congenital lymphedema, wing-like neck, etc. Afterwards this syndrome was found to be missing one of the sex chromosomes and its karyotype being 45XO. It has been ever said that Turner Syndrome occurs in 1/2500 newborn females and its incidence is increasing recently.[1] In addition, sudden death is sometime occurred in these infants and are needed to submit for forensic analysis in case there is suspicion about the death.

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2. Materials and method

Blood samples from an infant with Turner Syndrome and her parents were collected for DNA analysis. First, we performed X–Y Amelogenin DNA testing (106/112 bp) and five kinds of X STR tests (HPRTB, HumARA, STRX1, DXS6789, and DXS6807).

HVR (hypervariable regions) I and II of human mtDNA were analyzed by direct sequencing using ABI PRISM 377 DNA sequencer (Perkin Elmer) after cycle sequencing of Big Dye Primer method.

3. Results

X chromosomal STR analysis showed that this infant had only one X chromosome, supporting the diagnosis of pure Turner syndrome, excluding mosaic type. By repetitive testing, the possibility of mosaic was almost negative.

In the testing of inheritance pattern of X chromosome from the parents, the origin of inherited X was not easily determined because the parents interestingly have many identical alleles. So, it was suspected that the father and the mother were related in a way, that is,

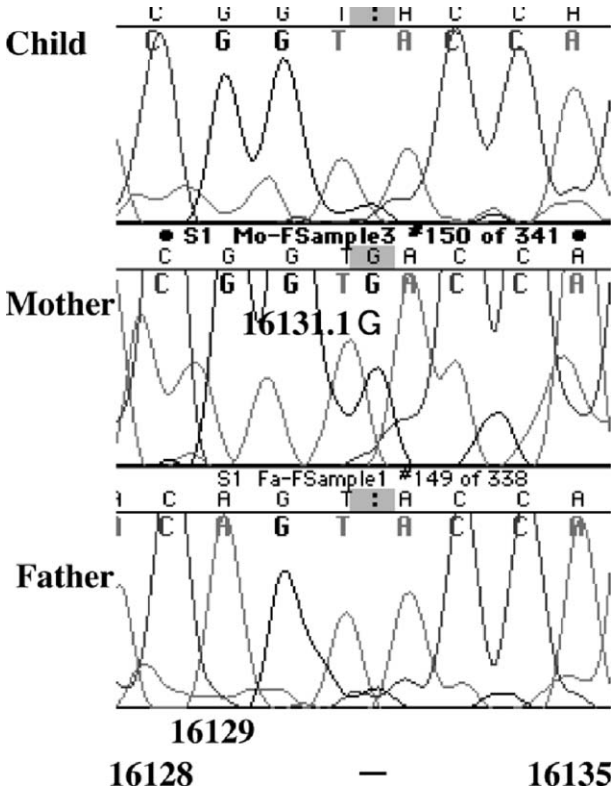

Fig. 1. The G insertion of nps16131 (mutation) in mother is disappeared in child. In addition, as for nps16129, the mother and child agrees in G, but father is A. It means that mitochondrial DNA sequence is different with child and father definitely, child and mothter slightly.

accidental intermarriage was not deniable. Fortunately, one (DXS 6789) out of five X-STRs tested showed that X chromosome of the infant was inherited from mother, in other words, a paternal sex chromosome was rejected.

Analysis of mtDNA HVR I and HVR II revealed that mtDNA of the infant was derived from mother. Curiously, mother's mtDNA has strange insertions, which were not found normal population yet. It was noted in G/C sequences of 16095-6, 16132-3 and 16150-1, disappeared in the child (Fig. 1).

Therefore, undeniable small difference of mtDNA between mother and the infant was recognized, that was, mutations of mother's mtDNA were excluded or repaired to usual type in child's mtDNA.

In conclusion, our data implied that mtDNA of maternal origin could generate some variations after fertilization.

4. Discussion

Turner's syndrome is an abnormality of a sex chromosome, and it is thought that the problem has no relevance with mtDNA. However, in our case, mutations were seen in mtDNA of mother, and it suggests that one cannot say that mt DNA has nothing to do with the genesis of sex chromosomal aberration [2,3].

It was thought that mtDNA and nuclear DNA have completely different origin, but our data suggest that both are related closely, and they might be relevant to each other. In more details, mtDNA might partially affect the fertilization and cell division. In our previous study, the similar phenomenon was found with Klinefelter's syndrome[4–6], supporting this hypothesis.

In mammals including humans, it has been believed that a child inherited mtDNA directly from the mother and constantly remained in its original state. However, it cannot be denied that there is a possibility that mtDNA can be varied by growth after having inherited the original DNA from the mother.

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