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Rapid prenatal detection of numerical chromosome disoders by quantitative flunorescence PCR:first clinical esperience

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1. Objective: We report the results of the first prospective study using quantitative fluorescence polymerase chain reaction (QF-PCR) for the rapid prenatal detection of common numerical chromosome aberrations. This molecular technique was applied to cell samples obtained from fetuses suspected of carrying chromosome abnormalities.

2. Methods: Amniotic fluid samples (n=33) and a placental biopsy (n=1), were analyzed by both QF-PCR and conventional karyotyping. These techniques were also applied to blood samples (n= 10) obtained from newborns with clinical features of Down syndrome. Multiplex QF-PCR assays were performed using small tandem repeat markers (STRs) specific for chromosomes 21, 18, 13 and X.

3.Results: All abnormal samples involving chromosomes 21 , 18 and 13 (4 cases of trisomy 21, 1 case of mosaicism of trisomy 21, 2 cases of trisomy 18. 1 ease of triploidy) were correctly identified. Two cases of gonosomal aneuploidies (47,XXY, 45,X) were not detected because of the homozygous. thus uninformative pattern of the X-chromosome markers . Another sample with a deletion (46,XX,7q-), that QF-PCR assays are not designed to identify, was not detected. Two samples could not be interpreted unequivocally due to maternal cell contamination. The remaining normal samples were correctly classified as disomic for chromosomes 21, 18 and 13 by QF-PCR

4.Conclusions: Our results suggest that QF-PCR is a rapid, accurate adjunct to conventional cytogenetic techniques for prenatal diagnosis.

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Mutation at nucleotide 1108 of the Fibroblast growth factor receptor 3 (FGFR3) in a case of thanatophoric dysplasia type I (TD1)

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Thanatophoric dysplasia (TD) is a Sporadic lethal type of skeletal dysplasia Featuring micromelia, decreased thoracic dimension and macrocephaly. To date, several kind of mutation in fibroblast growth factor receptor 3 (FGFR3) have been identified in TD1. We experienced a case of TD1 and underwent sequencing of exon 7,10 and stop codon of FGFR3 to identify the type of mutation.

TD1 was diagnosed by prenatal ultrasound at 25 weeks of gestation. The pregnancy was terminated and the diagnosis was confirmed by radiologic and histologic examinations. Genomic DNA was extracted and designated sequences of exon 7, 10 and sequence near the stop codon of FGFR3 were amplified by PCR. The sequencing was performed for each PCR products by dideoxy-terminator method.

Nucleotide transition from A to T was found in nucleotide 1108 which is a part of transmembrane domain, exon 10.

To date, mutation at nucleotide 742 of FGFR3 was identified in TD1 among asian. This case reveals mutation of FGFR3 other than mutation at nucleotide 742 of FGFR3 in TD1.