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Case Report

Prenatal diagnosis of microdeletion 16p13.11 combination with partial monosomy of 2q37.1-qter and partial trisomy of 7p15.3-pter in a fetus with bilateral ventriculomegaly, agenesis of corpus callosum, and polydactyly

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Abstract

Objective: To present a prenatal diagnosis of microdeletion 16p13.11 with partial monosomy of 2q37.1-qter and partial trisomy of 7p15.3-pter in a fetus with bilateral ventriculomegaly, agenesis of corpus callosum, and polydactyly.
Case Report: A 41-year-old well-being Taiwanese, nulligravida woman received amniocentesis at a gestational age of 18 weeks for advanced maternal age. The fetus' karyotype showed 46,XY,der(2)t(2;7)(q36.2;p15.1). Both parents also received cytogenetic examinations and the mother's karyotype revealed 46,XX,t(2;7)(2q36.2;p15.1). High-resolution ultrasound showed the fetus had bilateral ventriculomegaly, agenesis of corpus callosum, and polydactyly of the right hand. After the termination of this pregnancy, the whole genome oligonucleotide-base array comparative genomic hybridization (CGH) by using fetal skin cells demonstrated a 8.44-Mb deletion at 2q37.1 (234602276-243041305), a 22.8-Mb duplication (65558-22869338) at 7p15.3, and an additional 1.32-Mb deletion (14968855-16292235) at 16p13.11.
Conclusion: Array CGH is a useful tool not only to discover the genomic imbalance at the breakpoints as well as to detect unexpectedly complex rearrangements in other chromosomes. Our case also provided evidence that genomic aberration at chromosome 16p13.11 involves in the formation of polydactyly.

Keywords: agenesis of corpus callosum; microdeletion 16p13.11; polydactyly; ventriculomegaly

Introduction

Amniocentesis can detect inherited or *de novo* reciprocal translocations. Parents may be aware of their carrier status only after amniocentesis was performed. Jacobs and colleagues [1] found a prevalence of 0.218% for unbalanced structural rearrangements and a prevalence of 0.017% for unbalanced reciprocal translocations at prenatal diagnosis. The reciprocal translocations (products), which have gained or lost genetic materials, are called unbalanced reciprocal translocation. Most unbalanced translocations would produce such enormous genetic imbalance that the conceptus would be lost very early in pregnancy or even fail to implant. Chen and colleagues [2] reported in Taiwan that most unbalanced reciprocal translocations detected at amniocentesis were ascertained through abnormal ultrasound findings (44.8%, 13/29), and more than 80% of the fetus with unbalanced reciprocal translocations were associated with clinical abnormalities. Hillman and colleagues [3] reported an increasing of diagnostic yield up to 5.2% (95% confidence interval: 1.9–13.9) for genomic imbalance by array comparative

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genomic hybridization (CGH) more than conventional karyotyping when the referral indication was a structural malformation on ultrasound [3]. Here, we report a fetus with bilateral ventriculomegaly, agenesis of corpus callosum, and polydactyly of the right hand in prenatal ultrasound at gestational 20 weeks; the fetus had inherited unbalanced reciprocal translocation involving in chromosome 2q37.1 and 7p15.3 from the mother and also had an additional microdeletion of 16p13.11 identified by high-resolution array CGH.

Case report

A 41-year-old well-being Taiwanese, gravida 1, para 0 woman received a regular prenatal survey and received amniocentesis at 16 weeks of gestation because of her advanced maternal age. She and her husband denied any personal or family history of birth defect or abnormality and denied consanguinity. The fetal karyotype showed 46,XY,der(2)t(2;7)(q36.2;p15.1; Fig. 1A). Parents received further investigation and the mother's karyotype revealed 46,XX,t(2;7)(q36.2;p15.1; Fig. 1B). After abnormal karyotype revealed, high-resolution ultrasound showed bilateral ventriculomegaly, agenesis of corpus callosum (tear-drop sign) and polydactyly of right hand (Fig. 2A to C). The fetus revealed normal development: the estimated body weight was 406 g (50th percentile), biparietal diameter was 54 mm (90th percentile), femoral length was 34 mm (90th percentile), and abdominal circumference was 160 mm^2 [90th percentile]. Fetal magnetic resonance imaging performed at the same week showed similar results (Fig. 2D). After genetic counseling with parents, the termination of pregnancy was performed at 21 weeks of gestation. The appearance of the abortus revealed polydactyly over the right hand, a thin upper lip with a thick lower lip, and large anterior fontanelle (Fig. 3A to C). The parents refused autopsy of the fetus; thus, a central nervous system condition could not be confirmed. Further investigation of the abnormality was suggested and oral informed consent was obtained from the parents. Cultured fetal skin cell showed the same karyotype.

Fluorescent in situ hybridization (FISH) studies on the cultured fetal skin cells indicated the breakpoint on chromosome 2 is at 2q37.1 with a physical position of 235.24-235.44 Mb and the breakpoint on chromosome 7 is at 7p15.3 with a physical position 22.80-22.96 Mb (Fig. 4A and B). Oligonucleotide-based (oligo) aCGH (SurePrint H3 Human CGH Microarray Kit 4x180k; Agilent Technologies, Santa Clara, CA, USA) using culture fetal skin cell demonstrated a 8.44-Mb deletion at 2q37.1-qter (234602276-243041305), a 22.8-Mb duplication (65558-22869338) at 7p15.3-pter, and an additional 1.32-Mb interstitial deletion (14968855-16292235) at 16p13.11 (Fig. 4C and D).

Discussion

The present case of apparently unbalanced reciprocal translocations identified by conventional karyotype had multiple abnormalities, including bilateral ventriculomegaly, agenesis of corpus callosum (tear-drop sign), and polydactyly of the right hand. Array CGH helped to identify additional change of genomic changes at 16p13.11. Application of array CGH in the prenatal or postnatal setting to help detection of copy number variations, such as microdeletion and microduplication, is increasing [4]. Chen and coauthors [5] reported that array CGH had found an additional microduplication 2p12 in a case with balanced reciprocal translocation, 46,XY,t(3;11)(q14;q23). Chen and team [5] also described a fetus at 18 weeks' gestation with facial dysmorphism and hypospadias, and amniocentesis revealed a karyotype of 46,XY,del(4p16.1), and further array CGH analysis revealed a 6.5-Mb deletion at 4p16.3-p16.1, a 1.2-Mb microduplication at 8p22-p21.3, and a 1.1-Mb microduplication at 10p15.3 [6]. Therefore, precise definitions of simple or complex apparently balanced or imbalanced reciprocal translocations should include genome-wide aneuploidy diagnosis such as array CGH to find any subtle chromosome imbalance that may have occurred in other chromosomes.

Chromosome 16p13.11 recently has been reported as a region of recurrent microdeletion/duplication [7]. Microdeletion of 16p13.11 has been reported with multiple congenital

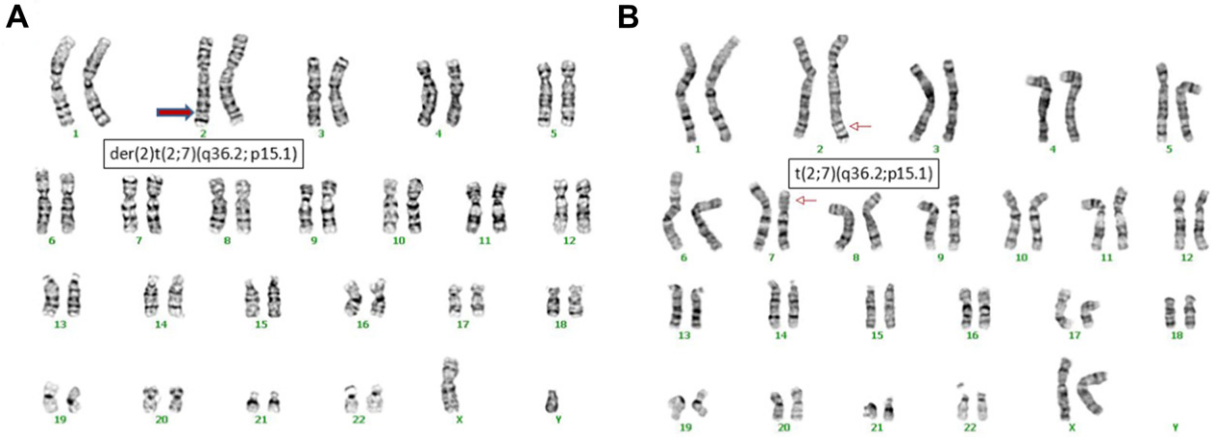

Fig. 1. (A) Fetal karyotype; (B) maternal karyotype.