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Case Report

Pure partial monosomy 3p (3p25.3 → pter): Prenatal diagnosis and array comparative genomic hybridization characterization

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Abstract

Objective: The purpose of this case report is to present prenatal diagnosis and molecular cytogenetic characterization of pure partial monosomy 3p (3p25.3 → pter) by array comparative genomic hybridization (aCGH) and quantitative fluorescent polymerase chain reaction (QF-PCR) on uncultured amniocytes.

Case Report: A 35-year-old, gravida 2, para 0, woman underwent amniocentesis at 19 weeks of gestation because of advanced maternal age. Her husband was 37 years of age. She had experienced one intrauterine fetal death. Amniocentesis during this pregnancy revealed a distal deletion of chromosome 3p. The parental karyotypes were normal. Prenatal ultrasonography findings were unremarkable. At 22 weeks of gestation, she underwent repeated amniocentesis, and aCGH investigation using CytoChip Oligo Array on uncultured amniocytes revealed a 9.29-Mb deletion of 3p26.3p25.3 [arr 3p26.3p25.3 (64,096–9,357,258 bp) ×1] encompassing the genes of *CHL1*, *CNTN4*, *CRBN*, *LRRN1*, *ITPR1,* and *SRGAP3,* but not involving the markers D3S1263 and D3S3594. Polymorphic DNA marker analysis on uncultured amniocytes showed a paternal origin of the deletion. Cytogenetic analysis of cultured amniocytes revealed a karyotype of 46,XX,del(3)(p25.3). At 24 weeks of gestation, prenatal ultrasonography findings of the brain, heart, and other internal organs were unremarkable. The pregnancy was subsequently terminated, and an 886-g female fetus was delivered with brachycephaly, hypertelorism, a short and thick nose, micrognathia and low-set ears.

Conclusion: In this case, aCGH has characterized a 3p deleted region with haploinsufficiency of the neurodevelopmental genes associated with cognitive deficit and mental retardation but without involvement of the congenital heart disease susceptibility locus, and QF-PCR has determined a paternal origin of the deletion. aCGH and QF-PCR help to delineate the genomic imbalance in prenatally detected *de novo* chromosome aberration, and the information acquired is useful for genetic counseling.

Keywords: 3p deletion syndrome; *CHL1*; *CNTN4*; *CRBN*; *ITPR1*; *LRRN1*; mental retardation; monosomy 3p; prenatal diagnosis; *SRGAP3*

Introduction

The 3p deletion syndrome (OMIM 613792) is a contiguous gene syndrome associated with partial monosomy 3p (3p25 → pter) and the characteristic phenotypic features of

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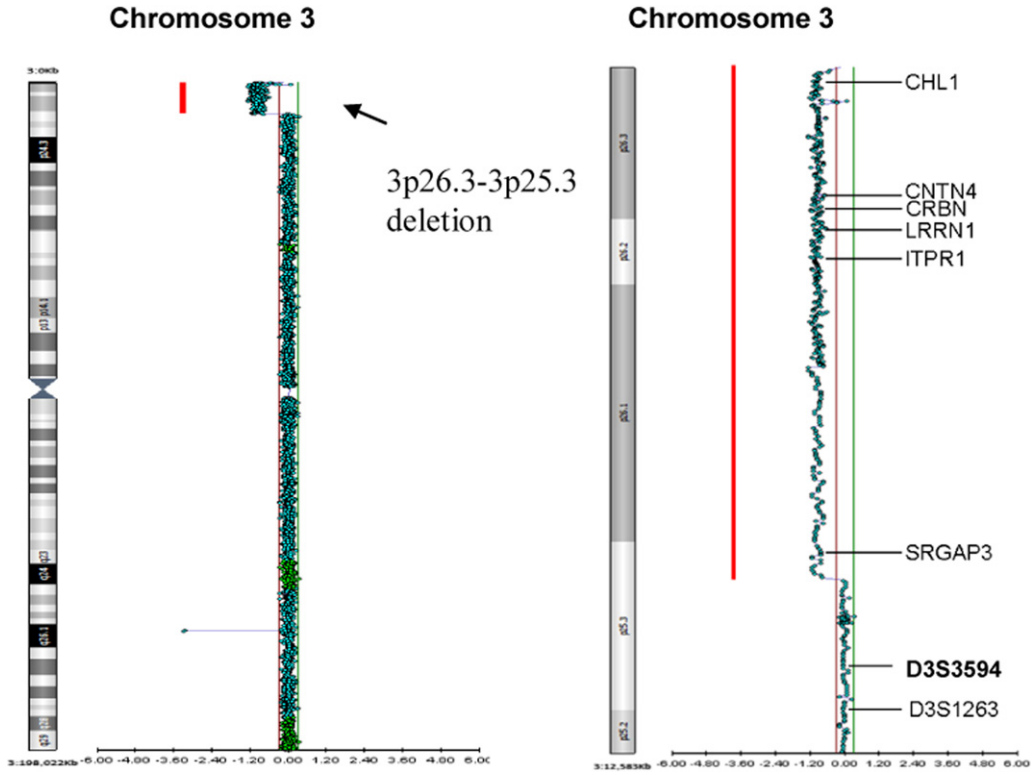

Fig. 1. Array comparative genomic hybridization investigation shows an ~ 9.29-Mb deletion of 3p25.3 → pter encompassing the genes of *CHL1*, *CNTN4*, *CRBN*, *LRRN1*, *ITPR1,* and *SRGAP3* but without involvement of the markers D3S1263 and D3S3594.

mental retardation, developmental delay, intrauterine growth restriction, micro- and brachycephaly, a triangular face, hypertelorism, epicanthus, upturned palpebral fissures, palpebral ptosis, frontal bossing, a short and thick nose, micrognathia, low-set ears, hypertrichosis, synophrys, long philtrum, and variable associated abnormalities, such as pectus excavatum, scoliosis, hypogenitalia, polydactyly, syndactyly, clinodactyly, atrioventricular septal defects, hiatal hernia, optic atrophy, polycystic renal dysplasia, and hypoplastic clavicles [1–4]. Here, we present our experience of prenatal diagnosis and array comparative genomic hybridization (aCGH) characterization of pure partial monosomy 3p (3p25.3 → pter) in a fetus.

Case report

A 35-year-old, gravida 2, para 0, woman underwent amniocentesis at 19 weeks of gestation because of advanced maternal age. Her husband was 37 years of age. She had experienced one intrauterine fetal death. Amniocentesis during this pregnancy revealed a distal deletion of chromosome 3p. The parental karyotypes were normal. Prenatal ultrasonography findings were unremarkable. At 22 weeks of gestation, she underwent repeated amniocentesis, and aCGH investigation using CytoChip Oligo Array (BlueGnome, Cambridge, UK) on uncultured amniocytes revealed a 9.29-Mb deletion of 3p26.3p25.3 [arr 3p26.3p25.3 (64,096–9,357,258 bp) ×1] encompassing the genes of *CHL1*, *CNTN4*, *CRBN*, *LRRN1*, *ITPR1,* and *SRGAP3* (Fig. 1). Polymorphic DNA marker analysis on uncultured amniocytes showed a paternal origin of the deletion (Fig. 2, Table 1). Cytogenetic analysis of cultured amniocytes revealed a karyotype of 46,XX,del(3)(p25.3; Fig. 3). At 24 weeks of gestation, prenatal ultrasonography

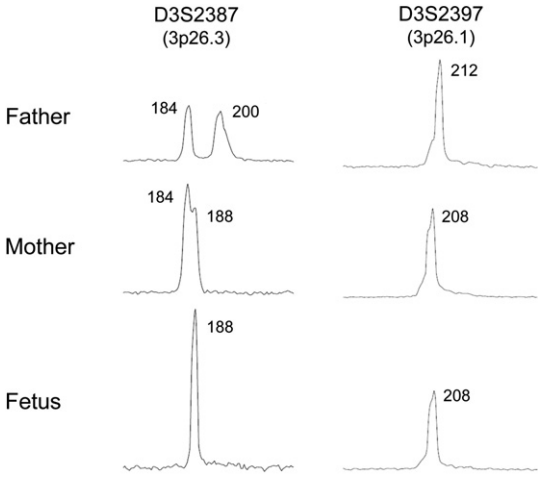

Fig. 2. Representative electrophoretograms of quantitative fluorescent polymerase chain reaction assays at short tandem repeat markers specific for chromosome 3p using uncultured amniocytes and parental DNAs. With the marker D3S2387 (3p26.3), only the allele of 188 bp (maternal) is present in the fetus. With the marker D3S2397 (3p26.1), only the allele of 208 bp (maternal) is present in the fetus. The results indicate a paternal origin of the deletion.