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Prenatal diagnosis of chromosome 3q25.32 and 12p11.22p11.1 microduplication with a favorable outcome

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Chromosomal abnormalities, including microdeletions and microduplications, have long been associated with abnormal developmental outcomes [1]. Recently, chromosomal microarray analysis has been introduced into routine practice for clinical diagnosis of chromosome imbalances, allowing for the identification of chromosome imbalances smaller than 5 Mb [2]. As a result, numerous copy number variations have been identified and their clinical significance needs to be clarified. Here we report the first inherited 3q25.32 and 12p11.22p11.1 microduplications with a favorable outcome.

A 39-year-old gravida-1-para-0 mother underwent amniocentesis at 18 weeks of gestation because of advanced maternal age. Her husband was 38 years old. There was no family history of birth defects or genetic diseases. Before amniocentesis, the expectant mother had undergone first trimester ultrasonography scanning and the results showed low risk (At 12 weeks of gestation, crown-rump length 55 mm, nuchal translucency 0.9 mm, nasal bone 2.8 mm and fetal heart rate 150 bpm). Conventional karyotyping revealed a normal karyotype of 46, XX (Fig. 1). Chromosomal microarray analysis (CMA) on uncultured amniocytes using the Affymetrix SNP 6.0 platform (Affymetrix, Inc., Santa Clara, CA) identified a 539 kb duplication, arr [hg19] 3q25.32 (158051049-158589843) x3 inherited from the mother and a 6.0 Mb duplication, arr [hg19] 12p11.22p11.1 (28833490-34835641) x3 from the father (Fig. 2). Both parents received a comprehensive physical examination, and the results were normal. Prenatal ultrasound showed no dysmorphisms or intrauterine growth restriction (IUGR) in the fetus. After genetic counseling, the parents decided to continue the pregnancy. At 39 weeks of gestation, a 3150 g phenotypically normal female baby was delivered vaginally. The infant was phenotypically normal at the 18-month checkup.

For both microduplications, we searched the Database of Genomic Variants (DGV, http://dgv.tcag.ca/) for the presence of these DGVs in the control population and found no previous reports. We also searched several clinical databases including DECIPHER (https://decipher.sanger.ac.uk) and ClinGen (https://clinicalgenome.org) and found no case with the exact duplications.

The microduplication in the region of 3q25.32 is 539 kb in size and includes five genes: RSRC1, MLF1, GFM1, LXN, and RARRES1. RARRES1 is a tumor suppressor gene associated with fatty acid metabolism, stem cell differentiation and is the most methylated loci in multiple cancers [3, 4]. Methylation at LXN and RARRES1 was highly correlated [5]. Increasing methylation was associated with decreased expression of both genes and worse clinical features [5].

The microduplication in the region of 12p11.22p11.1 is 6 Mb in size and includes 15 genes: FAR2, ERGIC2, TMTC1, IPO8, CAPRIN2, DDX11, FAM60A, ETFBKMT, H3F3C, BICD1, FGD4, DNM1L, YARS2, PKP2 and ALG10. There is no report supporting the triplosensitivity of these genes. Duplications in the region of 12p11 are associated with diverse phenotypes, ranging from normal phenotypes to severe physical defects in different organ systems [6]. In our case, the infant

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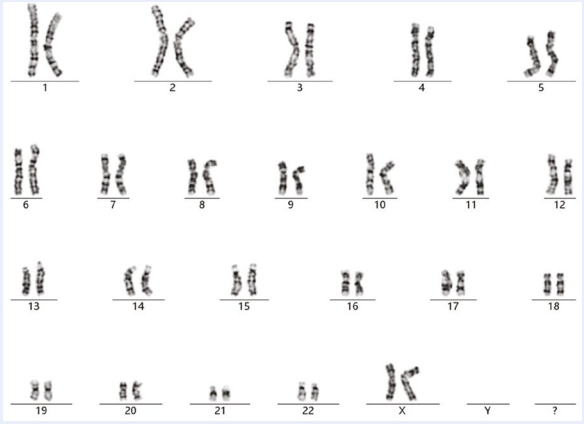

Figure 1. Karyotype of 46, XX

Figure 2. CMA analysis revealed a 539 kb duplication on chromosome arr [hg19] 3q25.32 (158051049-158589843) x3 and a 6.0 Mb duplication on chromosome arr [hg19] 12p11.22p11.1 (28833490-34835641) x3

is phenotypically normal at birth and develops normally in the first 18 months of life. The father who carries the same duplication was phenotypically normal.

To summarize, we present a case of inherited 3q25.32 and 12p11.22p11.1 microduplications with a favorable outcome. Our case presents evidence that these novel microduplications can be associated with a favorable outcome.

Conflict of interest

The authors have no conflicts of interest relevant to this article.

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Ethics approval and consent to participate

This study was approved by the Ethics Committee of Wuhan Blood Center. All patient guardians gave informed consent to this study.

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