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# A rare case of uniparental isodisomy of chromosome 7 without phenotypic anomalies

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## ABSTRACT

Uniparental disomy (UPD) is a well-known epigenomic anomaly with both copies of a homologous pair of chromosomes (or part thereof) inherited from the same parent. Unlike numerical or structural chromosomal aberrations, UPD has no effects on chromosome number or structure, thereby escaping cytogenetic detection. However, UPD detection could be performed by the microsatellite analysis or SNP-based chromosomal microarray analysis (CMA) method. UPD may cause diseases in humans by disrupting normal allelic expression of genes undergoing genomic imprinting, homozygosity in case of autosomal recessive traits, or mosaic aneuploidy. Here we present the first case of parental UPD for chromosome 7 with a normal phenotype.

**Keywords:** uniparental disomy; chromosomal microarray analysis; prenatal diagnosis

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A 38-year-old gravida 2 para 0 female had amniocentesis at pregnancy week 19 due to advanced maternal age. Cytogenetic assessment of amniocyte culture showed a normal karyotype, 46, XY. Chromosomal microarray analysis (CMA) assessing uncultured amniocytes was carried out with the Affymetrix CytoScan 750 K chip that comprises 200k SNP markers and 550k non-polymorphic. CMA revealed a 7.1-Mb uniparental isodisomy of chromosome 7, arr 7p22.3p22.1(44,166–7,152,131) × 2 hmz [GRCh37(hg19)] (Fig. 1) [1, 2]. Both parents had normal karyotypes and CMA findings. Microsatellite analysis indicated uniparental disomy (UPD) of chromosome 7 from the father. Laboratory findings of both parents were unremarkable. Ultrasound revealed the absence of facial dysmorphism or intrauterine growth restriction (fetal weight approximating 650 g and 1600 g at pregnancy weeks 24 and 30, respectively, with abdominal circumferences of 19.4 and 25.7 cm, head circumferences of 21.8 and 27.8 cm, femur lengths of 4.2 and 5.6 cm, and fetal heart rates of 150 and 145 bpm, respectively) [3]. Following genetic counseling, whole-exome sequencing (WES) was carried out to examine uncultured amniocytes. A Novaseq6000 platform (Illumina, USA), in the 150 bp pair-end sequencing mode, was utilized to sequence genomic DNA samples from the family members. The human reference genome (hg38/GRCh38) was utilized for aligning reads, with the Burrows-Wheeler Aligner tool. WES showed no homozygous mutations of reported recessive pathogenic genes for inherited diseases on chromosome 7p22. The parents opted for pregnancy continuation. At pregnancy week 39, a 3450 g boy was born *via* natural delivery, with Apgar scores of 9/9/10. He underwent full physical examination with no remarkable findings. At 36 months, he showed normal development (Intelligence Quotient, 112; weight, 14.8 kg; height, 98 cm; head circumference, 50.1 cm).

Maternal UPD of chromosome 7 is associated with Russell-Silver syndrome, which features pre- and post-natal growth retardation, macrocephaly and limb, body, and/or facial asymmetries [4]. Paternal UPD of chromosome 7 is extremely rare, with only seven cases reported so far [5]. Four of the latter cases were associated with autosomal-recessive diseases likely associated with growth retardation, two with an overgrowth phenotype, and one with cystic fibrosis and

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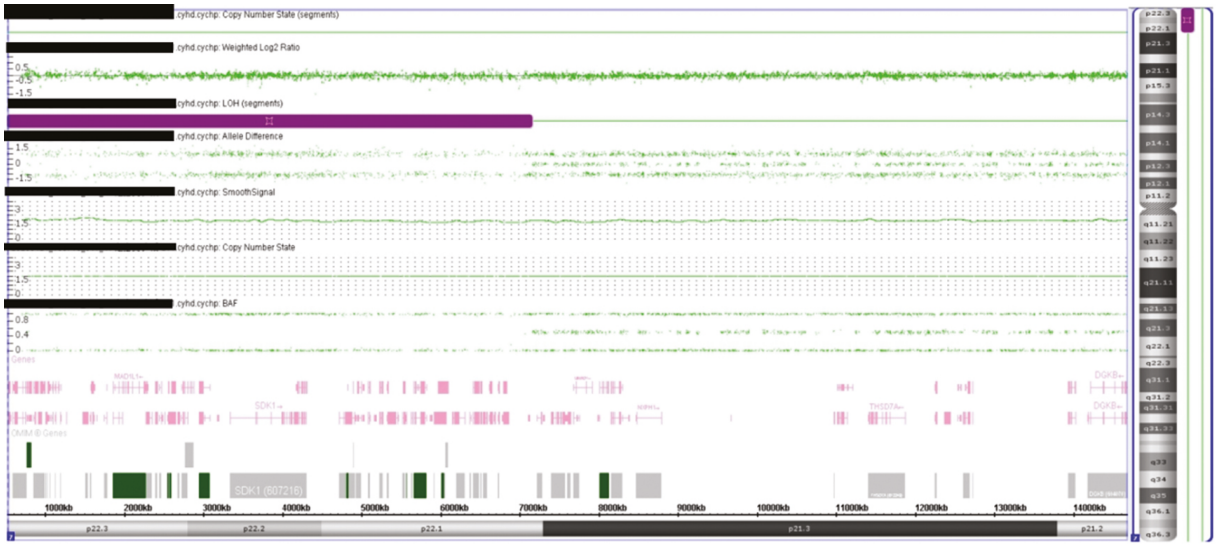


**Figure 1.** Uniparental isodisomy of chromosome 7, arr 7p22.3p22.1 (44,166–7,152,131) × 2 hmz [GRCh37(hg19)]

normal growth [5]. The present patient represents the first case of UPD of chromosome 7 with a normal phenotype.

UPD may cause several clinical phenotypes because of the homozygosity of recessive mutations or abnormal imprinting patterns [1]. Imprinting-related diseases affect epigenetic regulation and DNA methylation as well as histone modifications [5]. The broad utilization of the microsatellite analysis and SNP-based CMA assay has promoted UPD detection [2]. For most chromosomes, UPD causes no symptoms. However, for chromosomes 6, 7, 11, 14, 15 and 20, parent-of-origin or imprinting changes in gene expression exist in case of UPD, likely causing phenotypic anomalies [6]. Multiple suspected recessive pathogenic genes involved in inherited diseases are found on chromosome 7p22, including FAM20C, LFNG, and BRAT1. In the current boy, CMA and WES revealed no pathogenic mutations or homozygous recessive pathogenic genes.

Overall, we describe the first case of paternal UPD of chromosome 7 with no phenotypic anomaly.

## Article information and declarations

### *Ethics statement*

This research had approval from the Ethics Committee of Shiyan Renmin Hospital. The patient's guardians provided informed consent to the study.

### *Conflicts of interest*

There are no conflicts of interest relevant of this article.

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