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Case Report

# Prenatal diagnosis of a 3.2-Mb 2p16.1-p15 duplication associated with familial intellectual disability

Chih-Ping Chen [a, b, c, d, e, f, *], Schu-Rern Chern [b], Peih-Shan Wu [g], Shin-Wen Chen [a], Shih-Ting Lai [a], Tzu-Yun Chuang [a], Wen-Lin Chen [a], Chien-Wen Yang [b], Wayseen Wang [b, h]

[a] Department of Obstetrics and Gynecology, MacKay Memorial Hospital, Taipei, Taiwan
[b] Department of Medical Research, MacKay Memorial Hospital, Taipei, Taiwan
[c] Department of Biotechnology, Asia University, Taichung, Taiwan
[d] School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan
[e] Institute of Clinical and Community Health Nursing, National Yang-Ming University, Taipei, Taiwan
[f] Department of Obstetrics and Gynecology, School of Medicine, National Yang-Ming University, Taipei, Taiwan
[g] Gene Biodesign Co. Ltd., Taipei, Taiwan
[h] Department of Bioengineering, Tatung University, Taipei, Taiwan

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ABSTRACT

*Objective:* We present prenatal diagnosis of a 2p16.1-p15 duplication associated with familial intellectual disability, and we discuss the genotype–phenotype correlation.

*Case report:* A 22-year-old, primigravid woman underwent amniocentesis at 22 weeks of gestation because of a family history of intellectual disability. The woman and her two sisters had intellectual disability but no behavioral disorders. The intellectual disability was noted in at least one paternal aunt and six paternal cousins of the woman. Cytogenetic analysis revealed the karyotype of 46,XX in the fetus and the two women. Array comparative genomic hybridization (aCGH) analysis on the DNAs extracted from cultured amniocytes and the bloods of the woman and the her sister revealed a 3.244-Mb duplication of 2p16.1-p15 or arr 2p16.1p15 (58,288,588–61,532,538) × 3.0 [GRCh37 (hg19)] encompassing eight Online Mendelian Inheritance in Man (OMIM) genes of *VRK2*, *FANCL*, *BCL11A*, *PAPOLG*, *REL*, *PUS10*, *PEX13* and *USP34* in the fetus and the two women. Prenatal ultrasound findings were unremarkable. The woman elected to continue the pregnancy. A 3244-g female baby was delivered at term with neither craniofacial dysmorphism nor structural abnormalities.

*Conclusion:* aCGH is useful in prenatal diagnosis of inherited subtle chromosome imbalance in pregnancy with familial intellectual disability. Chromosome 2p16.1-p15 duplication can be associated with intellectual disability.



## Introduction

Chromosome 2p16-p15 deletion [Online Mendelian Inheritance in Man (OMIM) 612,513] is a well recognized neurodevelopmental syndrome characterized by delayed psychomotor development, intellectual disability, craniofacial dysmorphism of microcephaly, bitemporal narrowing, smooth and long philtrum, hypertelorism, downslanting palpebral fissures, broad nasal root, thin upper lip, and high palate, autistic behavior, short stature, pachygyria, hypoplastic corpus callosum and other brain malformations [1–10]. Various genes have been proposed for the association with the phenotypic features in chromosome 2p16.1-p15 deletion syndrome, *i.e.*, haploinsufficiency of *BCL11A* is responsible for neurodevelopmental disorders and dysmorphic facial features [8,9]. *VRK2* haploinsufficiency is responsible for autism and neuroectodermal developmental disorders [2], and *BCL11A* is responsible for language development [11]. Recently, Bagheri et al. [12] in a multifaceted analysis suggested that *XPO1*, *REL* and *BCL11A* are candidate genes for 2p16.1-p15 deletion syndrome.

Chromosome 2p16-p15 duplication, on the other hand, may present a less severe phenotype than chromosome 2p16-p15 deletion syndrome. Mimouni-Bloch et al. [13] previously reported a

* Corresponding author. Department of Obstetrics and Gynecology, MacKay Memorial Hospital, 92, Section 2, Chung-Shan North Road, Taipei 10449, Taiwan. Fax: +886 2 25433642, +886 2 25232448.
*E-mail address:* cpc_mmh@yahoo.com (C.-P. Chen).

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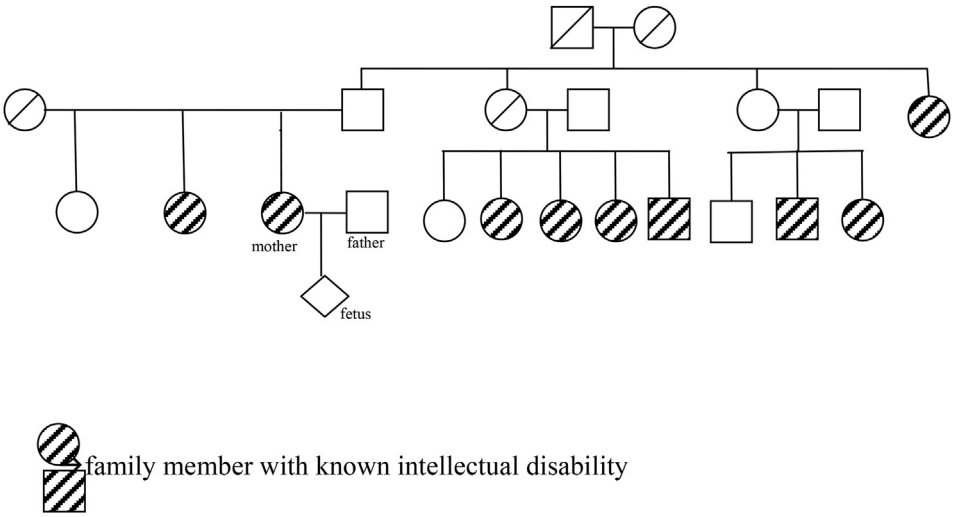


**Fig. 1.** A family pedigree of intellectual disability.

2p16.1-p15 duplication in a child with milder clinical phenotypes in comparison with the corresponding chromosome 2p16.1-p15 deletion syndrome. Here, we present prenatal diagnosis of a 2p16.1-p15 duplication associated with familial intellectual disability. Our presentation adds to the literature of 2p16.1-p15 duplication syndrome.

## Case report

A 22-year-old, primigravid woman underwent amniocentesis at 22 weeks of gestation because of a family history of intellectual disability. The woman and her two sisters had intellectual disability but no behavioral disorders. The woman and her sister had

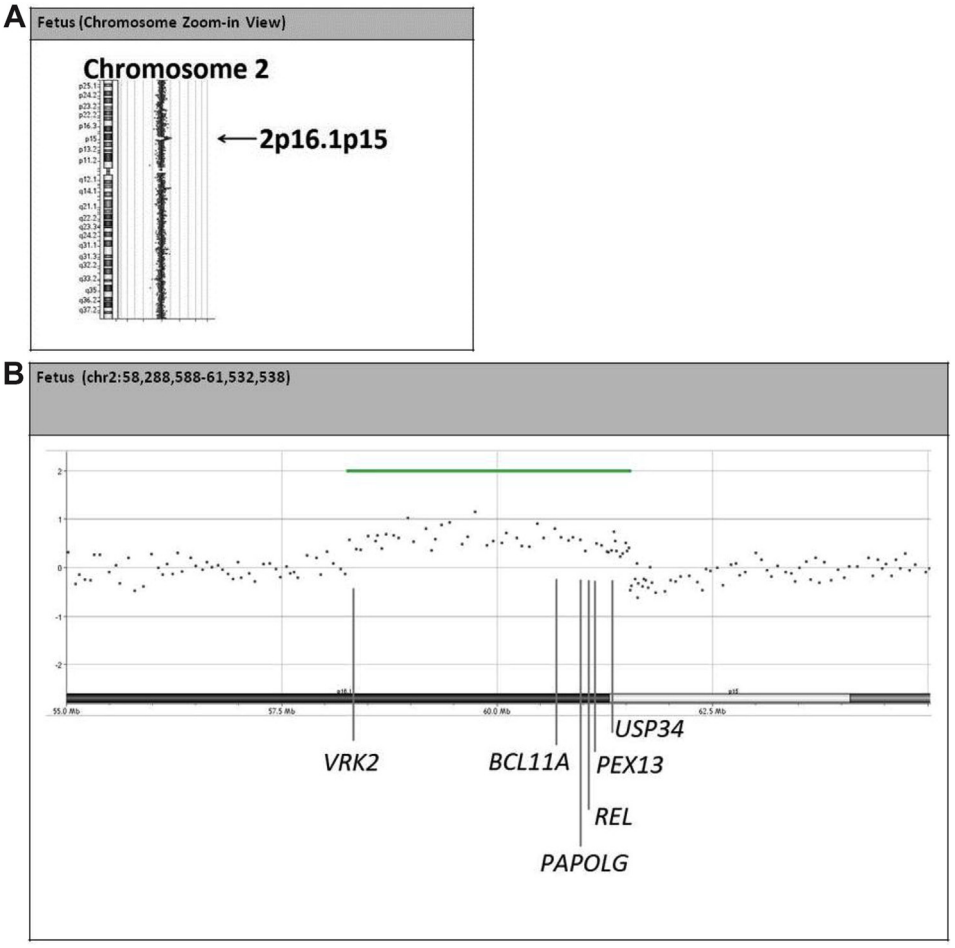


**Fig. 2.** Array comparative genomic hybridization (aCGH) on the DNA extracted from cultured amniocytes shows a 3.244-Mb duplication of 2p16.1-p15. (A) and (B) Chromosome zoom-in views.