Received: 13 October 2023 | Revised: 23 November 2023 | Accepted: 29 November 2023

DOI: 10.1002/ccr3.8315

CASE REPORT

Clinical Case Reports Open Access WILEY

Genetic analysis and prenatal diagnosis of a pedigree with developmental retardation due to paternal 8q/18q translocation

Chunyan Jin | **Xuefang Li** | **Jiao Chen** | **Zhiping Gu** | **Tianhui Xu**

Department of Medical Genetics and Prenatal Diagnosis, The Affiliated Taizhou People's Hospital of Nanjing Medical University (Taizhou People's Hospital), Taizhou, China

Correspondence
Tianhui Xu, Department of Medical Genetics and Prenatal Diagnosis, The Affiliated Taizhou People's Hospital of Nanjing Medical University (Taizhou People's Hospital), Taizhou, Jiangsu 225300, China.
Email: xth19921008@163.com

Key Clinical Message

Balanced reciprocal chromosomal translocation carriers will have greater risk to experience recurrent miscarriages, embryonic death, and infertility. We show the pedigree carrying a paternal karyotype which was reported first. This research helps to better understand the clinical manifestations and prognosis of patients with this rare chromosomal abnormality.

KEYWORDS

18q deletion syndrome, 8q duplication, 8q/18q translocation, balanced translocation, enrichment analysis, prenatal diagnosis

1 | INTRODUCTION

Reciprocal chromosomal translocation (RCT) is one of the most common human chromosomal abnormalities. Balanced RCT does not contain the variation in the number of chromosomes, but only the rearrangement of genetic material.[1] As we know, balanced RCT carriers will have greater risk to experience recurrent miscarriages, embryonic death, infertility, or giving birth to defective offspring.[2]

Copy number variants (CNVs) are also important causes of birth defects, resulting in various clinical manifestations, including growth and developmental abnormality, mental retardation, visceral malformation, and special facial features, etc.[3] At present, various syndromes are verified to be caused by CNVs, such as 22q11.2 deletion syndrome, Cri-du-chat syndrome, Williams syndrome, and so on.[4]

Above all, birth defects are important challenges affecting the quality of the birth population. Genetic counseling as well as prenatal diagnosis is effective method to decrease the rate of birth defects.[5]

In this study, we report the clinical findings detected in a Chinese pedigree (Figure 1). The proband was diagnosed by CMA to carry a 25.6 Mb duplication of 8q24.12-q24.3 and a 16.5 Mb deletion of 18q21.33-q23. Karyotype analysis showed that the karyotype of the proband is paternally inherited 46,XX,der(18)t(8;18)(q24.1;q21.3). This is the first of such a kind of karyotype to be reported. At the same time, the mother of the proband was pregnant for 18 weeks. CMA and karyotype analysis of amniotic fluid cells indicated that the fetus also carried the same karyotype as that of the proband. The couple decided to terminate the pregnancy after genetic counseling. Functional enrichment analysis of the genes involved was also carried out to find out the key genes causing the phenotype of the proband.

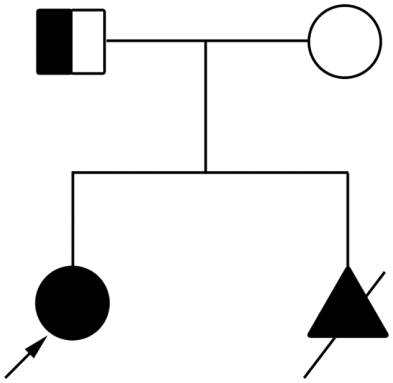

FIGURE 1 Pedigree of the family.

2 | MATERIALS AND METHODS

2.1 | Subjects

The proband is an 8-year-old girl with normal parents. She was delivered full-term of gestation by cesarean section with a birth weight of 3400 g and a length of 50 cm. There was no specific abnormality identified when she was delivered. While later, she was found to be unable to crawl at 1 year old. Clinical examination revealed signs of short statue, wide ocular distance, strabismus, slightly upturned and broad nose, thin upper lip, slightly hearing loss, protruding joints of the toes and being nearly unable to speak. The proband was the first child of her parents with no abnormality recognized during the pregnancy examination. The result of echocardiography performed at 20 months old was normal. MR examination of the brain in 2017 showed that the myelin sheath of the proband was underdeveloped. The mother of the proband had a history of four miscarriages. She was referred to the genetic counseling clinic because of abnormal pregnancy when she was 18 weeks pregnant with no abnormality found in the former pregnancy examination.

3 | METHODS

3.1 | Karyotype analysis of peripheral blood

0.5 mL of peripheral blood of proband and her parents were cultured for 72 h at 37°C with peripheral blood lymphocyte culture medium (Hangzhou Biozone Science Technology). After that, 80 μL colchicine (working concentration 10 μg/mL) was added and incubated for 65 min at 37°C. Hypotonic treatment was performed with 8 mL KCl solution (0.075 mol/L) before 1 mL fixed solution (methanol:glacial acetic acid = 3:1) was used for fixation. Total 50 Giemsa–Trypsin–Giemsa (GTG)-banded metaphase chromosomes were analyzed. For samples with abnormal chromosomes, a total of 100 metaphases were analyzed.

3.2 | Karyotype analysis of amniotic fluid

10 mL of amniotic fluid was obtained and cultured at 37°C with amniotic fluid culture medium (Guangzhou Baiyunshan Baidi Biotechnolgy). Before harvesting, 120 μL colchicine (working concentration 50 μg/mL) was added and incubated for 25 min at 37°C. After that, 2 mL pancreatin (Gibco) was added to stop digestion. Unlike peripheral blood, 6 mL of 1% sodium citrate solution was used for hypotonic treatment before 1 mL fixed solution (methanol:glacial acetic acid = 3:1) was added for fixation. Total 50 GTG-banded metaphase chromosomes were analyzed. For samples with abnormal chromosomes, a total of 100 metaphases were analyzed.

3.3 | Chromosomal microarray analysis

Genomic DNA was extracted from 200 μL peripheral blood or 10 mL amniotic fluid using QIAamp DNA Blood Mini Kit (QIAGEN). A total of 250 ng DNA was used to perform CMA using Affymetrix Cytoscan 750K Array (Affymetrix) followed by manufacturer's instructions. Raw data was processed by the software of ChAS (Affymetrix) and then analyzed referring to databases including Decipher, ISCA, ClinGen, OMIM, PudMed, and so on.

3.4 | Enrichment analysis

GO analysis was performed on the differential genes. The number of differential genes included in each GO entry was count. Hypergeometric distribution algorithm was used to calculate the significance of the enrichment of differential genes in each GO entry. The result of calculation will return a *p*-value with rich significance. The lower the value is the more significant it is statistically. The enrichment significance of each term in BP, CC, and MF was calculated by Fisher's exact test. The KEGG data is used to carry out the pathway analysis of differential genes, and the hypergeometric distribution algorithm is used to calculate the significance of the enrichment of differential genes in each pathway. The smaller the *p*-value, the higher the correlation between the corresponding pathway and this differential gene.

4 | RESULTS

4.1 | Genetic examination results of the family

Karyotype analysis of the proband showed 46,XX,der(18) karyotype with a derivative 18 chromosome. CMA identified a 25.6 Mb duplication of 8q24.12-q24.3 (ranging from position 120,721,382 to 146,295,771) and a 16.5 Mb deletion of 18q21.33-q23 (ranging from position 61,544,455 to 78,013,728) for the proband (Figure 2A,B) and normal CMA results for her parents (Figure 2E,F). To trace the origin of the derivative 18 chromosome and abnormal CNVs of the proband, karyotype analysis of her parents was performed. It was found that the mother showed 46,XX karyotype (Figure 3F), whereas the father was revealed to be a carrier of balanced RCT with 46,XY,t(8;18)(q23;q21.3) karyotype (Figure 3C,D). Taking together, the karyotype of the proband was finally to be recognized as 46,XX,der(18)t(8;18)(q24.1;q21.3)pat with a derivative 18 chromosome (Figure 3A,B). Results of CMA and karyotype analysis of amniotic fluid cells were the same as that of the proband (Figure 2C,D; Figure 3E). The couple decided to terminate the pregnancy after genetic counseling.

4.2 | Results of gene enrichment analysis

The GO analysis results of deleted OMIM gene showed that the first three terms of smallest *p*-value were serine-type endopeptidase inhibitor activity (Term ID: GO: 0004867), carboxypeptidase activity (Term ID: GO: 0004180), and translation from RNA polymerase II promoter (Term ID: GO: 0006366) (Figure 4A). Results of KEGG analysis showed that the first three paths with the smallest *p*-value were histidine metabolism (Term ID: path: hsa00340), beta-Alanine metabolism (Term ID: path: hsa00410), and arginine and line metabolism (Term ID: path: hsa00330) (Figure 4B). GO analysis results of duplicated OMIM genes showed that the first three terms with the smallest *p*-value were anchored component of membrane (Term ID:GO:0031225), C-terminal protein lipidation (Term ID:GO:0006501) and cell response to potassium ion (Term ID: GO: 0035865) (Figure 4C). The entry with statistical significance in the KEGG analysis results was aldosterone synthesis and secretione (Term ID:path:hsa04925) (Figure 4D).

5 | DISCUSSION

Carriers of balanced translocation usually have no phenotypic abnormality since there is no increase or decrease of genetic material. However, the tetrahedron will be formed during the association of homologous chromosome in meiosis, forming 18 gametes with only one normal and one balanced. While the other 16 are unbalanced, resulting in the risk of abortion, stillbirth, or deformity due to (part) monosomy or (part) trisomy.[6] As a result, genetic counseling for balanced RCT is particularly important. The key points of genetic counseling for these carriers mainly include: informing them of the probability of having a normal fetus, selecting the mode of pregnancy reasonably, and performing prenatal diagnosis during pregnancy.[7] In this study, the abnormal CNVs of the proband and the fetus are both caused by their father who is a carrier of balanced RCT. The previous four abortions of the mother of the proband should be related to the partial monosomy or trisomy caused by the paternally balanced RCT. The pregnancy termination of this time could be avoided if the family had genetic counseling earlier.

Only a few researches of 8q duplication have been reported, mainly involving 8q-ter duplication.[8] Phenotypes of 8q duplication were various. Digilio's research concluded that duplication of genes located on 8q could be an important cause of conotruncal cardiac defects.[9] Rezek et al. reported that duplication of 8q22.1-8q24.3 was associated with syndromic bilateral cleft lip/palate.[10] Macayran et al. suspected that duplication of 8q22.1-q24.1 was associated with bipolar disorder and speech delay.[11] Other reported phenotypes include dysmorphic facial features, renal malformations, hypoplastic and absent patella and so on.[12] The proband in this family presented a 25.6 Mb duplication of 8q24. It is reported that dysmorphic features of 8q24 duplication contains thin upper lip, slightly upslanting palpebral fissures, slightly upturned and broad nose, hypertelorism, micrognathia and mild psychomotor developmental delay.[13] Among 125 OMIM genes encompassed in 8q24 duplication (Table 1) of the proband, *TRAPPC9*, *TSTA3*, *KCNK9*, and *GPAA1* have been linked to developmental delay. *RECQL4* is suspected to be linked with cleft palate, while other genes such as *KCNQ3* and *GRINA* have been associated with epilepsy.[8,14] Four of these features were present for the proband, including thin upper lip, strabismus, broad nose and psychomotor developmental delay. No phenotype of cardiac abnormality or cleft lip and palate was showed for this proband.

Partial deletion of the 18q is a rare chromosomal abnormality which occurs in about 1/40,000 of live births.[15] The partial deletion of 18q of the proband reported in this study was caused by the balanced RCT of her father's chromosome 18 and chromosome 8. The mother of the proband was 18 weeks pregnant when referred to us. She decided to terminate the pregnancy because of the same karyotype of the fetus as that of the proband. The clinical phenotypes of the patients with 18q deletion were

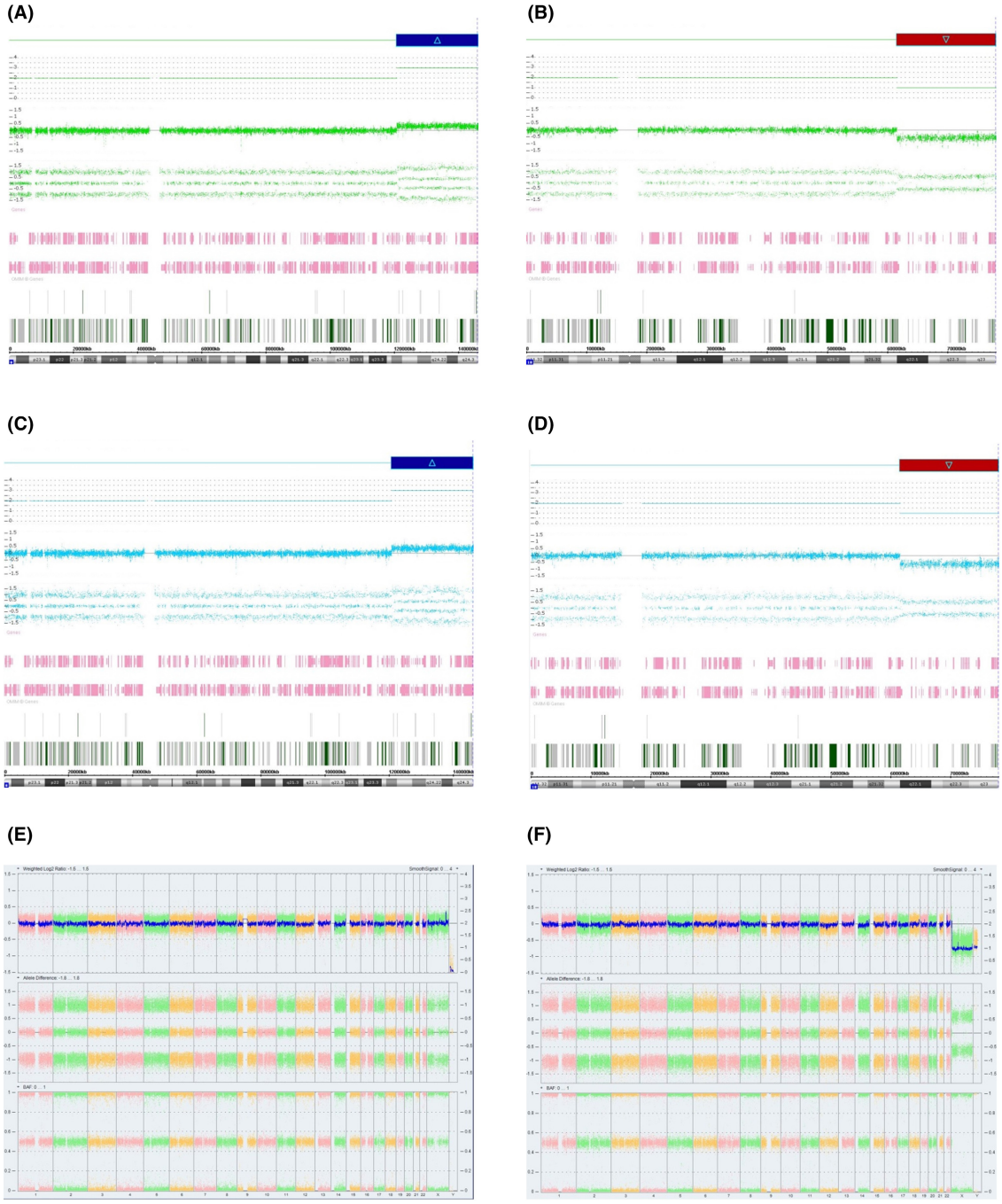

FIGURE 2 Chromosomal microarray analysis. (A) The result showed a 25.6 Mb duplication of 8q24.12-q24.3 of the proband denoted by a blue bar. (B) The result showed a 16.5 Mb deletion of 18q21.33-q23 of the proband denoted by a red bar. (C) The result showed a 25.6 Mb duplication of 8q24.12-q24.3 of the fetus denoted by a blue bar. (D) The result showed a 16.5 Mb deletion of 18q21.33-q23 of the fetus denoted by a red bar. (E) The normal CMA result of the proband's mother. (F) The normal CMA result of the proband's father.

different due to the location and length of the deletion fragments. It is difficult to analyze the correlation between genotype and phenotype since the 18q partial deletion fragments are relatively large.[16] Some critical regions have been reported to be associated with several features, including delayed myelination (18q22.3-q23), GH deficiency (18q22.3-q23), congenital aural atresia (18q22.3), microcephaly (18q21.33), short stature (18q12.1-q12.3, 18q21.1-q21.33, 18q22.3-q23).[17] Several key genes have been reported as well. *MBP* is recognized to be an important gene to maintain the stability of myelin structure and function. *GALRL* may be related to the change of growth hormone level. *NFATCL* is related to endocardial tissue development. *SALL3* and *TSHZ1* may be related to cleft lip and palate phenotype. *TSHZ1* gene has also been associated with congenital vertical talus.[18–22]

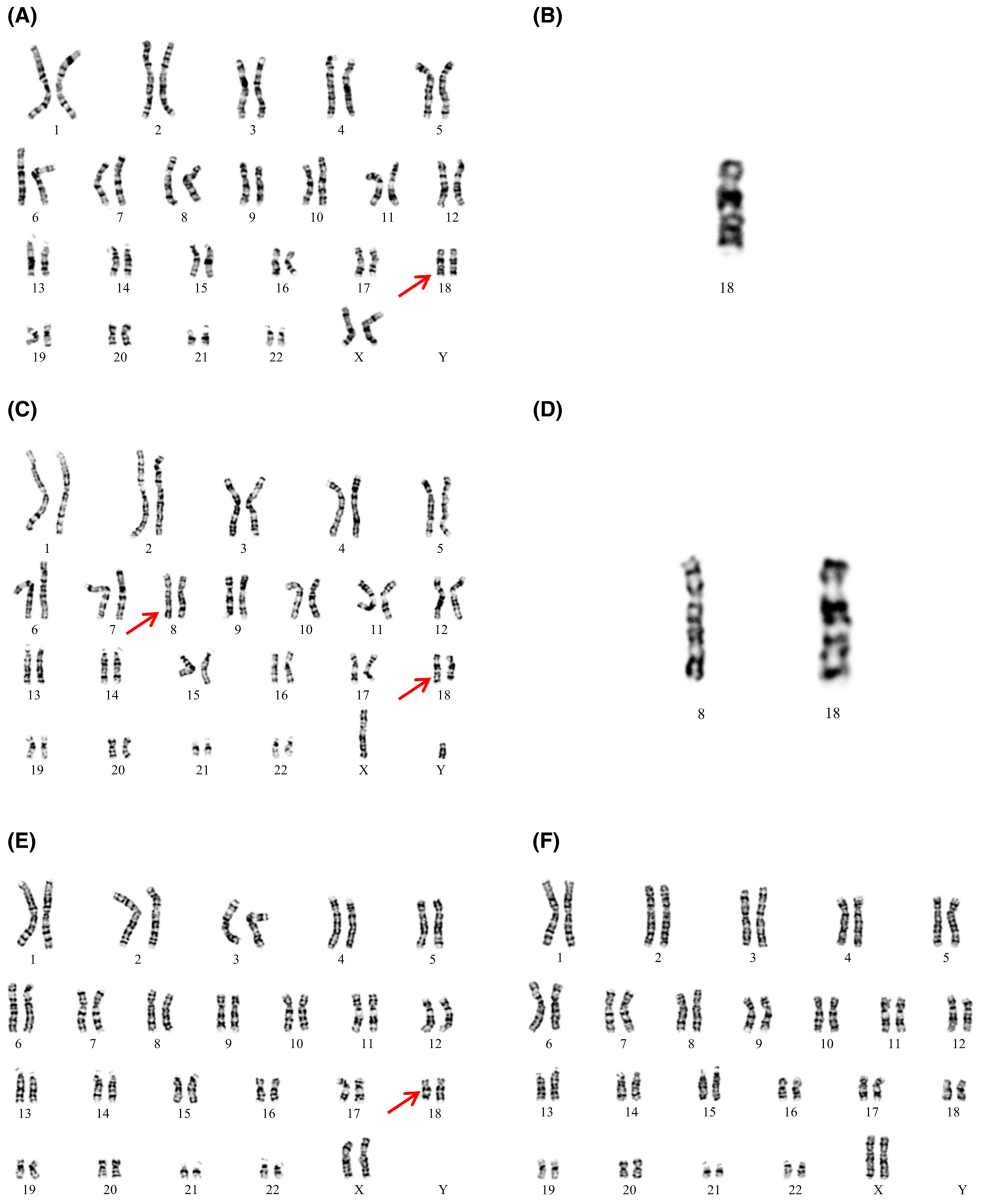

FIGURE 3 Conventional karyotype analysis. (A) The G-banding result of the proband showed 46,XX,der(18)t(8;18)(q24.1;q21.3)pat karyotype with the derivative 18 chromosome denoted by a red arrow. (B) The proband's partial karyotype of derivative 18 chromosome. (C) The G-banding result of the proband's father showed 46,XY,t(8;18)(q23;q21.3) karyotype with the RCT between the long arm of chromosomes 8 and 18 denoted by a red arrow respectively. (D) Partial karyotype of the proband's father with t(8;18)(q23;q21.3). (E) The G-banding result of the fetus showed 46,XX,der(18)t(8;18)(q24.1;q21.3)pat karyotype with the derivative 18 chromosome denoted by a red arrow. (F) The G-banding result of the proband's mother showed 46,XX karyotype.

The deletion of 18q21.33q23 for the proband covers most of the above key pathogenic areas and important genes, therefore overlaps some of the above phenotypic characteristics. Main phenotypes of the proband involve short statue, wide ocular distance, strabismus, slightly upturned and broad nose, thin upper lip, slightly hearing loss, protruding joints of the toes and being nearly unable to speak, and dysmyelination. Cody et al. reported that patients had various features even with same deletions, implying the existence of penetrance with associated phenotypes.[16] In deed, ultrasonic examination of the proband's mother indicated that the fetus had begun to show the phenotype of lateral ventricle widening during the process of waiting for amniocentesis results.

Derivative chromosomes of this case due to translocations involving 8q and 18q have never been reported previously. We compared the phenotypes of this proband with other 8q duplication or 18q deletion patients (Table 2). It is difficult to determine which CNVs cause the phenotype

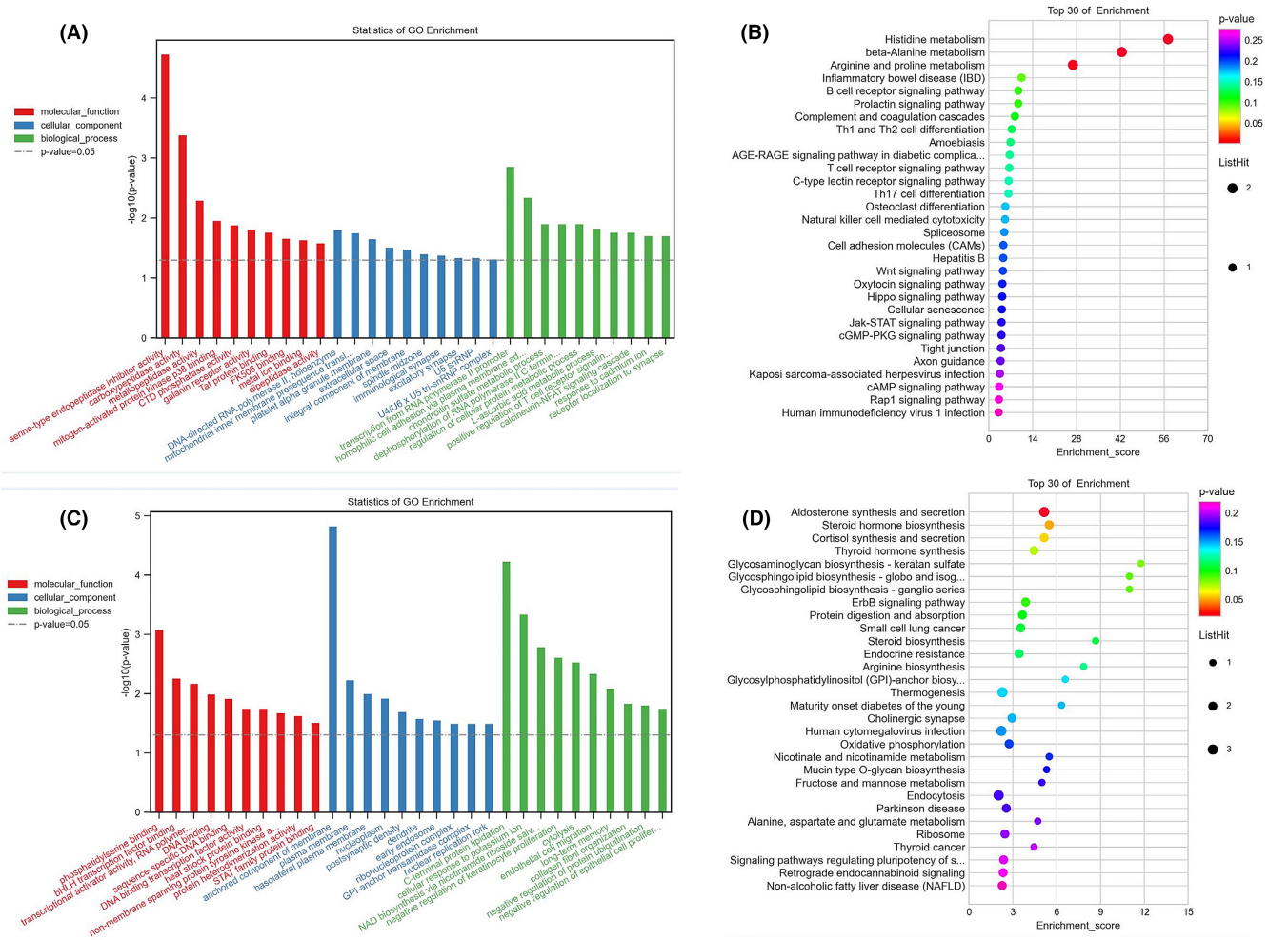

FIGURE 4 Enrichment analysis. (A) The GO enrichment results of deleted OMIM gene. (B) The KEGG enrichment results of deleted OMIM gene. (C) The GO enrichment results of duplicated OMIM gene. (D) The KEGG enrichment results of duplicated OMIM gene.

of the proband according to the existing information since some traits of 8q duplication and 18q deletion were both observed. In addition, this proband was nearly unable to speak. This phenotype has never been mentioned to be associated with 8q duplication or 18q deletion before. Above all, this research adds to the literature that duplication of 8q24.12-q24.3 and deletion of 18q21.33-q23 may result in variable phenotypes even with the same CNVs and reflects the importance of prenatal diagnosis and genetic counseling.

Magnetic resonance examination showed that myelin sheath of the proband was poorly developed. 80%–90% of the brain myelin sheath growth retardation was related to genetic factors including gene mutation, chromosome abnormality, protease metabolism abnormality, enzyme deficiency, etc. The main symptoms include brain growth retardation, lagging behind peers in sports and language. Dysplasia of brain myelin sheath will lead to cognitive impairment of patients, especially for young children. For example, there are obstacles in memory, great difficulties in learning new things, and inattention.[23]

The enrichment results of deleted OMIM gene showed that it was related to the metabolic process of various enzymes and amino acids. The normal metabolism of amino acids is an important basis for life activities. All tissues and cells of the body can carry out amino acid metabolism, including deamination, decarboxylation, ammonia metabolism, oxidative decomposition capacity, and other processes as well as participating in protein synthesis. Liver, kidney, and muscle are important tissues and organs for amino acid metabolism, playing important roles in the metabolism of amino acids in the body. Abnormal amino acid metabolism is closely related to the occurrence of human diseases.

The number of missing and repetitive fragments containing various number of genes of the proband was large. It is considered that the possible missing genes have a

TABLE 1 OMIM genes identified by CMA of dup 8q24 and del 18q21.33q23.

Microarray nomenclature	Size (kbp)	Cytoband start	Cytoband end	OMIM genes count	OMIM genes
arr[hg 19] 8q24.12q24.3(120,721,382-146,295,771)x3	25574	q24.12	q24.3	125	*TAF2*, *DSCC*, *DEPTOR*, *COL14A1*, *MRPL13*, *MTBP*, *SNTB1*, *HAS2*, *HAS2-AS1*, *ZHX2*, *DERL1*, *ZHX1*, *ATAD2*, *FBXO32*, *ANXA13*, *TMEM65*, *TRMT12*, *RNF139*, *NDUFB9*, *MTSS1*, *SQLE*, *WASHC5*, *NSMCE2*, *TRIB1*, *FAM84B*, *PCAT1*, *PCAT2*, *PRNCR1*, *CASC19*, *CCAT1*, *CASC21*, *CASC8*, *POU5F1B*, *CASC11*, *MYC*, *PVT1*, *CCDC26*, *GSDMC*, *FAM49B*, *ASAP1*, *ADCY8*, *EFR3A*, *OC90*, *HHLA1*, *KCNQ3*, *LRRC6*, *TG*, *SLA*, *PTCSC1*, *WISP1*, *NDRG1*, *ST3GAL1*, *ZFAT*, *KHDRBS3*, *COL22A1*, *KCNK9*, *TRAPPC9*, *CHRAC1*, *AGO2*, *PTK2*, *DENND3*, *GPR20*, *PTP4A3*, *ADGRB1*, *ARC*, *JRK*, *PSCA*, *LY6K*, *SLURP1*, *LYNX1*, *LY6D*, *GML*, *CYP11B1*, *CYP11B2*, *LY6E*, *LY6H*, *GPIHBP1*, *GLI4*, *TOP1MT*, *RHPN1*, *MAFA*, *GSDMD*, *NAPRT*, *EEF1D*, *PYCR3*, *TSTA3*, *FAM83H*, *SCRIB*, *PUF60*, *NRBP2*, *EPPK1*, *PLEC*, *MIR661*, *PARP10*, *GRINA*, *SPATC1*, *OPLAH*, *EXOSC4*, *GPAA1*, *CYC1*, *SHARPIN*, *MAF1*, *SCX*, *BOP1*, *HSF1*, *DGAT1*, *SCRT1*, *FBXL6*, *SLC52A2*, *CPSF1*, *SLC39A4*, *VPS28*, *TONSL*, *CYHR1*, *KIFC2*, *FOXH1*, *PPP1R16A*, *GPT*, *RECQL4*, *ARHGAP39*, *ZNF34*, *RPL8*, *ZNF7*, *COMMD5*, *ZNF16*
arr[hg 19] 18q21.33q23(61,544,455-78,013,728)x1	16,469	q21.33	q23	35	*SERPINB2*, *SERPINB10*, *HMSD*, *SERPINB8*, *LINC00305*, *CDH7*, *CDH19*, *DSEL*, *TMX3*, *DOK6*, *CD226*, *RTTN*, *SOCS6*, *CBLN2*, *NETO1*, *FBXO15*, *TIMM21*, *CYB5A*, *FAM69C*, *CNDP2*, *CNDP1*, *ZNF407*, *TSHZ1*, *ZNF516*, *ZNF236*, *MBP*, *GALR1*, *SALL3*, *ATP9B*, *NFATC1*, *CTDP1*, *KCNG2*, *TXNL4A*, *ADNP2*, *PARD6G*

TABLE 2 Clinical manifestations of the proband and others patients with dup (8q22-24) and 18q deletion.

	Concolino et al.	Wheeler 2010 et al.	Cody et al.	This study
Chromosomal imbalance	8q22.2-q24.3 duplication	8q23.3-q24.21 duplication	18q deletion	8q24.12-q24.3 duplication and 18q21.33-q23
Short stature	+	+	71%	+
Facial features				
Wide ocular distance	−	+	N/A	+
Strabismus	−	N/A	38%	+
Broad nose	N/A	N/A	N/A	+
Long philtrum	+	−	N/A	+
Palate abnormality	N/A	N/A	50%	−
Ears abnormality	+	+	77%	−
Thin upper lip	+	N/A	N/A	+
Micrognathia	+	+	N/A	−
Microcephaly	N/A	N/A	N/A	−
Neurologic anomalies				
Delayed myelination	N/A	N/A	100%	+
Hypotonia	−	+	93%	+
Mental retardation	+	+	100%	+
Hearing loss	−	+	75%	+
Seizures	−	−	20%	−
Spasticity	N/A	N/A	N/A	−
Limb anomalies				
Cubitus valgus	−	N/A	N/A	−
Equinovarus	−	+	N/A	−
Distal phalanges hypoplasia	+	−	64%	−
Abnormal toes	+	−	57%	+
Birth defects				
Congenital cardiac defects	+	−	54%	N/A
Frontal meningocele	+	−	N/A	−
Bifid uvula	−	+	N/A	−

Note: +: The feature is present. −: The feature is not present. N/A: not assessed or not available.

greater impact on the phenotype of the proband through enrichment analysis although the missing fragments are smaller than the duplicates. *n* conclusion, it needs further research that which gene or genes play a major role in the pathogenesis.

AUTHOR CONTRIBUTIONS

Chunyan Jin: Conceptualization; formal analysis; writing – review and editing. **Xuefang Li:** Data curation; project administration. **Jiao Chen:** Project administration. **Zhiping Gu:** Data curation; resources. **Tianhui Xu:** Software; writing – original draft; writing – review and editing.

ACKNOWLEDGMENTS

We thank nurse Pei Yu for drawing peripheral blood of the patient and her parents. We also thank the patient and her family for taking part in this research.

FUNDING INFORMATION

No funding.

CONFLICT OF INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author.

ETHICS STATEMENT

This study was approved by the Affiliated Taizhou People's Hospital of Nanjing Medical University (Taizhou People's Hospital).

CONSENT

Written informed consent was obtained from the parents.

ORCID

Tianhui Xu https://orcid.org/0000-0002-0610-7250

REFERENCES

1. Chen CP, Lin CJ, Chern SR, et al. Prenatal diagnosis and molecular cytogenetic characterization of a de novo unbalanced reciprocal translocation of der(9)t(9;14)(p24.2;q32.11) associated with 9p terminal deletion and 14q distal duplication. *Taiwan J Obstet Gynecol*. 2016;55:596-601.
2. Zhao X, Xu H, Zhao C, Li L. Developmental retardation due to paternal 5q/11q translocation in a Chinese infant: clinical, chromosomal and microarray characterization. *J Genet*. 2019;98:77.
3. Liang D, Peng Y, Lv W, et al. Copy number variation sequencing for comprehensive diagnosis of chromosome disease syndromes. *J Mol Diagn*. 2014;16:519-526.
4. Weise A, Mrasek K, Klein E, et al. Microdeletion and microduplication syndromes. *J Histochem Cytochem*. 2012;60:346-358.
5. Munne S. Analysis of chromosome segregation during preimplantation genetic diagnosis in both male and female translocation heterozygotes. *Cytogenet Genome Res*. 2005;111:305-309.
6. Scriven PN, Handyside AH, Ogilvie CM. Chromosome translocations: segregation modes and strategies for preimplantation genetic diagnosis. *Prenat Diagn*. 1998;18:1437-1449.
7. Lin XL, Xie FN, Tang SH, et al. Prenatal diagnosis and clinical counseling for fetal chromosomal reciprocal translocations. *Zhonghua Yi Xue Yi Chuan Xue Za Zhi*. 2013;30:612-615.
8. Bonaglia MC, Giorda R, Tenconi R, et al. A 2.3 Mb duplication of chromosome 8q24.3 associated with severe mental retardation and epilepsy detected by standard karyotype. *Eur J Hum Genet*. 2005;13:586-591.
9. Digilio MC, Angioni A, Giannotti A, Dallapiccola B, Marino B. Truncus arteriosus and duplication 8q. *Am J Med Genet A*. 2003;121a:79-81.
10. Rezek RF, Rodrigues Abbas AA, Forte Mazzeu J, Duarte Miranda SM, Velloso-Rodrigues C. A rare interstitial duplication of 8q22.1-8q24.3 associated with syndromic bilateral cleft lip/palate. *Case Rep Dent*. 2014;2014:730375.
11. Macayran JF, Brodie SG, Rao PN, et al. Duplication 8q22.1-q24.1 associated with bipolar disorder and speech delay. *Bipolar Disord*. 2006;8:294-298.
12. Wheeler PG. 8q23-q24 duplication—further delineation of a rare chromosomal abnormality. *Am J Med Genet A*. 2010;152a:459-463.
13. Concolino D, Iembo MA, Moricca MT, et al. A de novo 8q22.2-24.3 duplication in a patient with mild phenotype. *Eur J Med Genet*. 2012;55:67-70.
14. Nguyen TTM, Murakami Y, Sheridan E, et al. Mutations in GPAA1, encoding a GPI transamidase complex protein, cause developmental delay, epilepsy, cerebellar atrophy, and osteopenia. *Am J Hum Genet*. 2017;101:856-865.
15. Cody JD, Ghidoni PD, DuPont BR, et al. Congenital anomalies and anthropometry of 42 individuals with deletions of chromosome 18q. *Am J Med Genet*. 1999;85:455-462.
16. Cody JD, Hasi M, Soileau B, et al. Establishing a reference group for distal 18q-: clinical description and molecular basis. *Hum Genet*. 2014;133:199-209.
17. Feenstra I, Vissers LE, Orsel M, et al. Genotype-phenotype mapping of chromosome 18q deletions by high-resolution array CGH: an update of the phenotypic map. *Am J Med Genet A*. 2007;143a:1858-1867.
18. Mark PR, Radlinski BC, Core N, Fryer A, Kirk EP, Haldeman-Englert CR. Narrowing the critical region for congenital vertical talus in patients with interstitial 18q deletions. *Am J Med Genet A*. 2013;161a:1117-1121.
19. Cody JD, Hale DE, Brkanac Z, Kaye CI, Leach RJ. Growth hormone insufficiency associated with haploinsufficiency at 18q23. *Am J Med Genet*. 1997;71:420-425.

20. Ott T, Parrish M, Bond K, Schwaeger-Nickolenko A, Monaghan AP. A new member of the spalt like zinc finger protein family, Msal-3, is expressed in the CNS and sites of epithelial/mesenchymal interaction. *Mech Dev*. 2001;101:203-207.
21. Ragancokova D, Rocca E, Oonk AM, et al. TSHZ1-dependent gene regulation is essential for olfactory bulb development and olfaction. *J Clin Invest*. 2014;124:1214-1227.
22. Wu B, Wang Y, Lui W, et al. Nfatc1 coordinates valve endocardial cell lineage development required for heart valve formation. *Circ Res*. 2011;109:183-192.
23. Stadelmann C, Timmler S, Barrantes-Freer A, Simons M. Myelin in the central nervous system: structure, function, and pathology. *Physiol Rev*. 2019;99:1381-1431.

How to cite this article: Jin C, Li X, Chen J, Gu Z, Xu T. Genetic analysis and prenatal diagnosis of a pedigree with developmental retardation due to paternal 8q/18q translocation. *Clin Case Rep*. 2023;11:e8315. doi:10.1002/ccr3.8315