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CASE REPORT

Unbalanced Derivative Chromosome 15 From Maternal T(10;15)(P15;Q13) In A Child with Congenital Heart Disease, Dysmorphism, And Global Developmental Delay

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Abstract: Rearrangements involving chromosome 15q11–q13 are well known in neurodevelopmental disorders and imprinting syndromes, while 10p15 anomalies have been associated with developmental delay and speech/language impairment. Unbalanced 10;15 rearrangements are rare, and genotype–phenotype correlations remain incompletely defined. We describe a male child with a karyotype 47,XY,+der(15)t(10;15)(p15;q13)mat, indicating an additional derivative chromosome 15 derived from a maternal balanced reciprocal translocation. Clinically, he presented with a large subaortic ventricular septal defect, mitral regurgitation, dysmorphic craniofacial features, global developmental delay, recurrent respiratory infections, and mild left hydronephrosis. Neuroimaging showed mild ventricular and sulcal prominence without structural malformations. Initial cytogenetic analysis reported 47,XY,+15,del(15)(q21); subsequent parental karyotyping refined the abnormality as 47,XY,+der(15)t(10;15)(p15;q13)mat. This case illustrates a rare unbalanced derivative chromosome 15 involving 10p15 and 15q13 with multisystem involvement. The phenotype is most likely attributable to partial trisomy of distal chromosome 10 (10p15.3–pter) and chromosome 15 (15pter–q13), leading to dosage imbalance of genes within the 15q11–q13 imprinted region and 10p15 neurodevelopmental loci. These findings support a role for combined 10p15/15q13 dosage imbalance in developmental delay, dysmorphism, congenital heart disease, and recurrent respiratory morbidity, underscoring the importance of parental karyotyping and detailed genomic characterization.

Keywords: Unbalanced translocation, Genotype-phenotype correlation, Global Developmental Delay

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1 Introduction

Copy number and structural rearrangements of chromosome 15q11–q13, particularly involving the Prader–Willi/Angelman critical region, are associated with a spectrum of neurodevelopmental, behavioral, and epilepsy phenotypes and classic imprinting disorders. [1-4]. Recurrent microdeletions and microduplications of 15q11–q13, including those encompassing UBE3A, GABRB3, GABRA5, GABRG3, and other imprinted genes (e.g., MKRN3, MAGEL2, NDN, ATP10A), arise from non-allelic homologous recombination between low-copy repeats [1,3,4].

Structural abnormalities of 10p15.3 have more recently been delineated as a recognizable microdeletion and microduplication syndrome with global developmental delay, speech and language impairment, hypotonia, and variable dysmorphism [5-7]. Candidate genes include ZMYND11 and DIP2C, with ZMYND11 haploinsufficiency strongly implicated in intellectual disability and language delay [6,7]. However, interchromosomal translocations involving 10p15 and 15q11–q13 are exceptional, and only a handful of individuals with unbalanced 10;15 rearrangements have been described [8-10].

We report a male patient with a karyotype 47,XY,+der(15)t(10;15)(p15;q13)mat, who presented with dysmorphic features, global developmental delay, congenital heart disease, recurrent respiratory infections, and mild renal and skeletal anomalies. We discuss the potential contribution of dosage changes in 10p15 and 15q11–q13 to the observed phenotype and highlight the counseling implications of maternally inherited balanced translocations leading to unbalanced offspring.

2 Case Presentation

Perinatal and Family History The patient was a male infant born at term by cesarean section due to maternal preeclampsia. Birth weight was 4.5 kg (large for gestational age). The neonatal period was reportedly uneventful, and he was discharged home with his mother. The mother was 30 years old at the time of pregnancy and had gestational hypertension diagnosed at seven months, with irregular follow up. The father was 37 years old and clinically healthy. The couple were non consanguineous and had two other healthy daughters. There was no family history of congenital heart disease or neurodevelopmental disorders. There was no known history of recurrent miscarriages, same condition or infertility in the extended family.

Initial cardiac presentation was at four months of age, as during a routine pediatric consultation, a cardiac murmur was detected. Echocardiography revealed a large subaortic ventricular septal defect (VSD). Since early infancy, the patient experienced recurrent chest infections, often requiring hospitalization and several intensive care unit (ICU) admissions, although no specific immunological work up was documented.

Phenotypic evolution By one year and six months, the child presented with apparent developmental delay and facial dysmorphism. On examination craniofacial dysmorphic features included a bulbous nose with a wide nasal base, a depressed nasal bridge, a long philtrum, and large, asymmetric, protruding ears with abnormal folding. Additional external findings included bilaterally wide great toes and bilateral retractile testes. Neurological examination demonstrated normal muscle tone, power, and deep tendon reflexes, with no evidence of focal neurological deficits, movement disorders, or overt ataxia. Chest examination showed bilateral equal air entry with wheezing, consistent with recurrent lower respiratory involvement, but no focal consolidation was noted at the time of examination. Abdominal examination revealed a soft, lax abdomen without hepatosplenomegaly. The anthropometric assessment revealed weight and head circumference below the 5th percentile, with length/height approximately at the 5th percentile.

At one year and 11 months of age, the patient continued to exhibit global developmental delay. He was able to sit and crawl independently at one year and fourth months and began cruising around furniture at approximately 18 months; however, independent walking had not been clearly documented by one year and 11 months. Fine motor development was delayed, with the ability to transfer objects between hands using a palmar grasp but no established pincer grasp at this age. In terms of language and social development, he spoke approximately 7–10 single words without forming two-word phrases, although he recognized his name and responded to simple commands, indicating relatively preserved receptive language. Overall, these findings are consistent with global developmental delay, more prominently affecting motor and expressive language domains, with comparatively better social engagement.

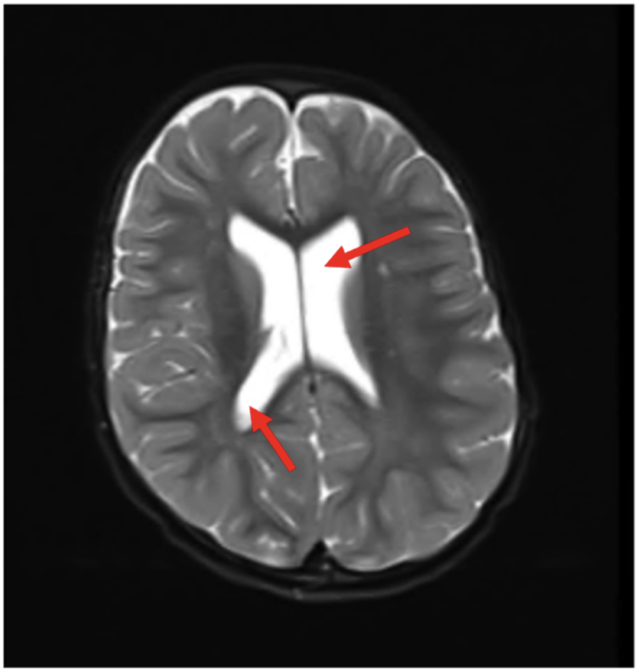

Figure 1. Brain MRI showing mild prominence of the cerebral ventricles and cortical sulci

Imaging and Ancillary Investigations: Follow-up echocardiography performed at one year and six months of age demonstrated a large ventricular septal defect (VSD) associated with significant mitral regurgitation. The patient subsequently underwent corrective cardiac surgery consisting of VSD closure and mitral valve repair. Postoperative echocardiography confirmed complete closure of the VSD with mild to moderate residual mitral regurgitation, and no significant pulmonary hypertension was documented in the available records. The patient continued to require multidisciplinary cardiology follow up for surveillance of residual mitral regurgitation and overall cardiac function.

Brain magnetic resonance imaging (MRI) revealed

mild prominence of the cerebral ventricles and cortical sulci, without evidence of structural malformations, signal abnormalities, or lactate peak on MR spectroscopy as shown in figure 1. These findings were interpreted as mild, nonspecific cerebral volume loss or changes related to developmental delay, without overt cerebral malformation.

Abdominal ultrasonography demonstrated mild dilatation of the left renal pelvis with mild left-sided hydronephrosis, with no additional renal or urinary tract anomalies identified. A limited skeletal survey showed frontal bossing, a slightly depressed nasal bridge as shown in figure 2, with no major limb anomalies or vertebral segmentation defects observed. Immunological, and endocrine evaluations were not comprehensively documented in the available medical records.

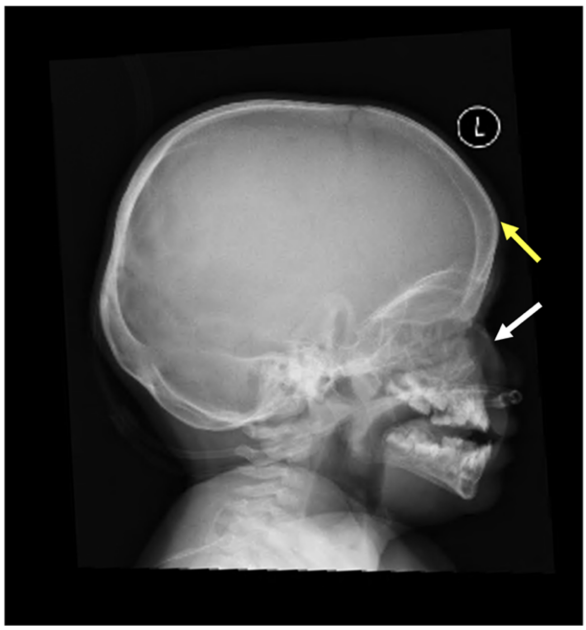

Figure 2. Skeletal survey including skull showing frontal bossing and slightly depressed nasal bridge

Cytogenetic Evaluation: Cytogenetic analysis by fluorescence in situ hybridization (FISH) and karyotyping initially reported a chromosomal abnormality: 47,XY,+15,del(15)(q21). Subsequent refined chromosomal analysis characterized the karyotype as: 47,XY,+der(15)t(10;15)(p15;q13)mat (Figure 3). This indicated an extra derivative chromosome 15 originating from an unbalanced maternal reciprocal translocation between 10p15 and 15q13. The father had a normal karyotype while the mother was confirmed to be a carrier of a balanced t(10;15), as shown in figure 4 (A, B).

The child's karyotype, 47,XY,+der(15)t(10;15)(p15;q13)mat, is consistent with a rare unbalanced derivative chromosome 15 resulting from a maternally inherited translocation between chromosomes 10 and 15. This rearrangement leads to partial trisomy included the distal short arm of chromosome 10 (10p15.3–pter) and trisomy of chromosome 15 spanning from pter to q13, which most likely underlies the patient's multisystem clinical phenotype.

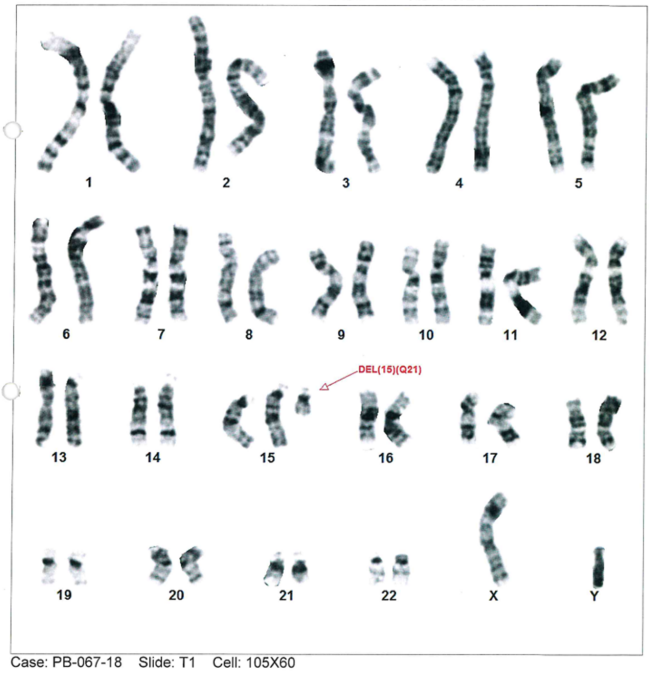

Figure 3. Conventional karyotype analysis of the proband

Candidate Genes in 15q11–q13 and 10p15: The 15q11–q13 region contains several neurodevelopmentally important genes, including GABRB3, GABRA5, and GABRG3 (GABA_A receptor subunits), and UBE3A, an imprinted gene implicated in Angelman syndrome and autism spectrum phenotypes. Additional genes within or adjacent to the imprinted domain, such as ATP10A, MKRN3, MAGEL2, NDN, CYFIP1, NIPA1, NIPA2, and HERC2, may contribute to neurodevelopmental abnormalities and growth disturbances when dosage is altered. Duplications of 15q11–q13 are associated with hypotonia, developmental delay, speech impairment, intellectual disability, autistic features, and occasionally dysmorphic features or seizures. Our patient's global developmental delay, expressive language delay, and subtle craniofacial

dysmorphism are consistent with a 15q11–q13 duplication phenotype, though no seizures were observed. The 10p15.3 region has been linked to developmental delay, speech impairment, behavioral abnormalities, and variable dysmorphism. Notable genes include ZMYND11, a transcriptional regulator involved in chromatin remodeling and neuronal development, and DIP2C, implicated in neuronal differentiation. Broader 10p15 duplications may involve genes such as KLF6, PFKP, IDI1, and ADARB2, whose contribution to neurodevelopment is less well defined. Partial trisomy of 10p15 in our patient likely results in dosage gain of one or more of these genes, potentially contributing to developmental delay, growth disturbance, and structural anomalies, including mild renal anomalies.

3 Discussion

We report a male child with a rare unbalanced derivative chromosome 15 resulting from a maternally inherited t(10;15)(p15;q13), presenting with a complex multisystem phenotype. The karyotype resulted in partial trisomy of distal 10p15.3–pter and 15pter–q13, contributing to global developmental delay, expressive language impairment, subtle motor delay, and multisystem involvement including congenital heart disease and recurrent respiratory infections.

The child exhibited global developmental delay, with pronounced expressive language impairment and relatively preserved social engagement. This mixed neurodevelopmental profile aligns with the established phenotypes of 15q11–q13 duplications—often associated with hypotonia, speech delay, intellectual disability, and autistic features—and with emerging reports of 10p15 microdeletion/duplication syndromes affecting ZMYND11, DIP2C, and other dosage-sensitive genes implicated in neuronal development [1,5–7]. While data on 10p15 duplications remain limited, increased gene dosage may disrupt neurodevelopmental circuits, contributing to the observed deficits.

Craniofacial dysmorphism, including a bulbous nose with a wide base, depressed nasal bridge, long philtrum, and large asymmetric protruding ears, fits within the spectrum described for both 15q11–q13 duplications and 10p15 CNVs. Skeletal findings such as bilateral wide halluces may reflect dosage imbalance of transcriptional regulators affecting connective tissue or growth plate development. Although neither chromosomal region has a pathognomonic facial gestalt, these features add to the phenotypic spectrum of unbalanced 10;15 rearrangements.

The patient's large subaortic VSD with significant mitral regurgitation necessitating early surgical correction is notable. While congenital heart defects are not a common manifestation of 15q11–q13 duplications, sporadic cases have been reported, and the contribution of 10p15 dosage changes remains uncertain [11,12]. This observation suggests that cardiovascular surveillance may be warranted in children with unbalanced rearrangements involving these loci.

Recurrent lower respiratory infections may be secondary to the hemodynamic burden of the VSD and mitral regurgitation, or reflect vulnerability associated with developmental delay. Mild left hydronephrosis and renal pelvic dilatation may be coincidental, though renal anomalies have been sporadically described in other chromosomal copy number variants. Brain MRI revealed mild prominence of the ventricles and cortical sulci without structural malformations, consistent with global developmental delay driven by neurodevelopmental circuitry rather than gross brain malformations.

The maternal balanced translocation highlights the importance of parental karyotyping in cases of structural chromosomal abnormalities. Balanced carriers are at risk of producing offspring with unbalanced rearrangements and complex multisystem phenotypes. Genetic counseling should address recurrence risk, options for prenatal testing, and consideration of preimplantation genetic diagnosis in future pregnancies.

Although the breakpoints differ from previously reported 10;15 rearrangements, our patient's phenotype extends the spectrum of unbalanced translocations involving these loci. Prior reports describe developmental delay, language impairment, and dysmorphic features, but our case additionally demonstrates congenital heart disease and recurrent respiratory infections, underscoring the variable multisystem involvement possible with such chromosomal imbalances [8–10].

4 Conclusion

In summary, this case contributes to the literature by demonstrating that unbalanced t(10;15)(p15;q13) can result in a complex neurodevelopmental and multisystem phenotype. Recognition of such rearrangements has important implications for clinical management, surveillance, and genetic counseling.

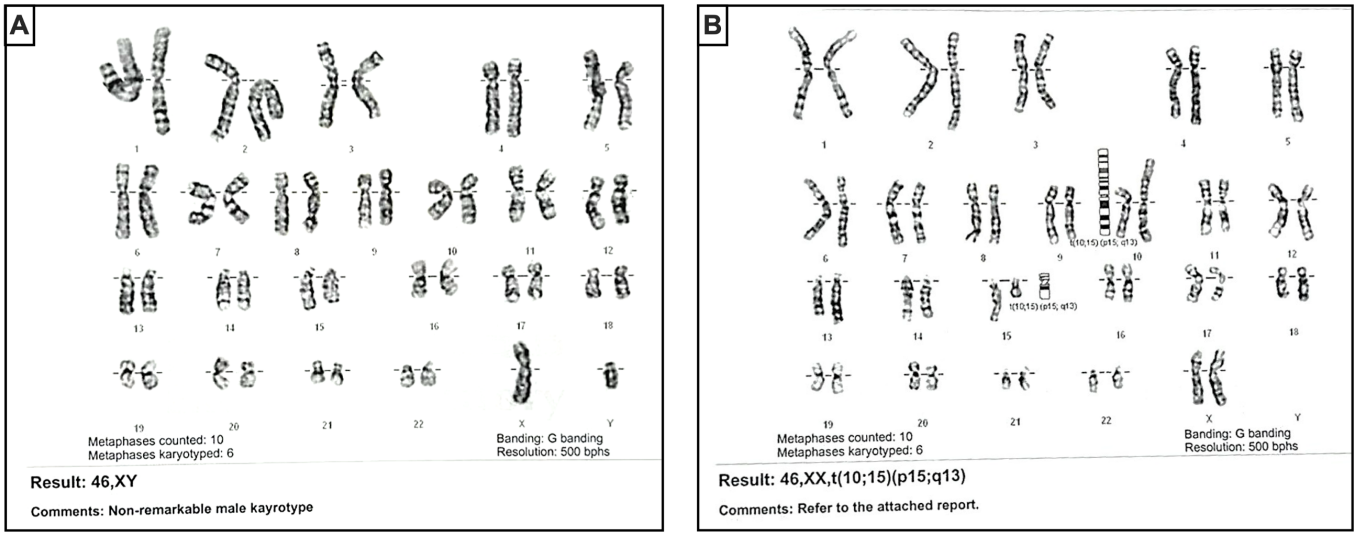

Figure 4. Karyotype analysis of the parents: (A) father; (B) mother.

The maternal balanced translocation t(10;15)(p15;q13) underscores the importance of parental karyotyping in children with structural chromosomal rearrangements. Balanced carriers are at increased risk of having offspring with unbalanced karyotypes and complex phenotypes. Genetic counseling should address recurrence risk, options for prenatal diagnosis, and preimplantation genetic testing for future pregnancies.

This report is limited by the absence of high-resolution chromosomal microarray or genome sequencing data, which would have allowed precise delineation of duplicated or deleted segments and more accurate genotype–phenotype correlations. Additionally, standardized developmental and behavioral assessments, as well as long-term neurocognitive follow-up, were not available. Despite these limitations, the case provides valuable clinical and cytogenetic information, contributing to the limited literature on unbalanced 10;15 rearrangements and highlighting key features that may guide targeted cytogenetic evaluation.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Ethical Approval

Written informed consent was obtained from the patient to be included in this study. The case report was approved by Research Ethical Committee- Unit of Biomedical Ethics-King Abdulaziz University (Reference number 263-25 dated 31 December 2025).

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