EXPANDING THE CLINICAL SPECTRUM OF INTELLECTUAL DISABILITY ASSOCIATED WITH *MECP2* DUPLICATION

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Xq28 duplication or MECP2 duplication syndrome (MDS) is a rare X-linked genetic disorder characterized by intellectual disability (ID), neurodevelopmental disorders (NDDs), recurrent respiratory infections, abnormal facial features, and progressive neurological decline. Several challenges exist in the clinical identification of MDS, particularly given that most male patients inherited the chromosomal abnormality from asymptomatic or mildly symptomatic carrier mothers. The objective of our familial case series was to provide a clinical description of four males with intellectual disability across two generations in a Vietnamese family with MECP2 duplication syndrome. Chromosomal microarray analysis (CMA) was used to confirm the molecular abnormality and its segregation within the family. This familial case series illustrates typical and variable manifestations of MDS, especially changes observed from the fetal to the neonatal and adolescent period, which is essential, especially in diseases reported as progressive neurological decline, such as MECP2.

Keywords: MECP2 duplication syndrome, intellectual disability, duplication.

I. INTRODUCTION

The MECP2 gene (OMIM #300005), located on the terminal of the long arm of chromosome X (Xq28), encodes the methyl-CpG-binding protein 2, capable of binding specifically to methylated DNA - a critical regulator of gene expression.[1,2] To date, numerous studies have demonstrated its role in neuronal maturation and synaptic regulation. In mice, MeCP2 regulates growth differentiation factor 11 (Gdf11), which losing one copy can cause multiple neurobehavioral deficits.[3] In humans, variants in MeCP2-interacting TCF20/PHF14 complex components have recently been increasingly recognized as central factors associated with neurodevelopmental disorders.[4]

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Understanding alterations in MECP2 protein across developmental stages will explain the diverse clinical phenotypes observed in MECP2-related disorders. Its expression starts in mid-gestation and continues increasing until 10 years old. In adulthood, MeCP2 reaches its plateau as a critical factor in the maintenance of neuronal function.[5] Alterations in MECP2 level, either through loss or gain of *MeCP2* function, can cause neurodevelopmental disorders as Rett syndrome (RTT; MIM 312750) or MECP2 duplication syndrome (MDS; MIM 300260), respectively. Despite overlapping phenotypes, RTT-specific symptoms are developmental regressions in females and MDS-specific symptoms represent a distinct clinical entity characterized by moderate to severe intellectual disability, epilepsy, recurrent infections, and progressive neurological symptoms in males.[6-8]

In contrast to other methyl-CpG binding domain family members (MECP2, MBD1,

MBD2, MBD3, and MBD4), MECP2 is X-linked and subject to X inactivation.[1] Most reported MECP2 duplication cases are males with maternally inherited duplications, while female carriers are typically asymptomatic or mildly affected due to X-inactivation.[9] Chromosomal microarray analysis (CMA), with a detection resolution of approximately 300-400 kb for copy number changes, is currently the most suitable genetic technique for detecting MDS.[8]

To our knowledge, there is no case of MDS reported in Vietnam, and few studies have documented its longitudinal phenotypic evolution, particularly in Asian populations. The objective of this study is therefore to describe the genetic and phenotypic spectrum of familial MDS cases across developmental stages. Comprehensive knowledge of its typical and variable manifestations is essential for accurate diagnosis, effective genetic counseling, and age-appropriate management and follow-up, particularly given its progressive neurological nature.

II. MATERIALS AND METHODS

A familial case series was conducted at the Center of Clinical Genetics and Genomics, Hanoi Medical University Hospital between April 2025 and June 2025. Six family members with clinical features suggestive of neurodevelopmental disorder or X-linked inheritance were invited for clinical evaluation and genetic testing. We performed a comprehensive assessment including a report of detailed perinatal and postnatal history and an evaluation of dysmorphic features and developmental milestones from both observation, and parents' report.

We performed chromosomal microarray analysis test on two separate occasions, both using the GenetiSure Cyto CGH Microarray Bundle 8×60K (G5982C) (Agilent Technologies, Santa Clara, CA, USA). The average probe spacing was approximately 60 kb, and data were analyzed using Agilent Cytogenomics Software v5.4 with the GRCh38/hg38 genome build as reference. Copy-number variants (CNVs) were called using standard manufacturer thresholds (log_2 ratio ± 0.3; minimum of five consecutive probes). Segregation testing was subsequently performed in available family members (II.10, II.11, III.11, III.12). CNVs were classified according to the ACMG/ClinGen 2020 technical standards for CNV interpretation. We interpreted and reviewed all variants independently. CNVs identified by CMA were later validated by CNV analysis derived from exome sequencing data generated on the MGI NEXome XP Panel v1.0 platform.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethical Review Board of Hanoi Medical University (Ethical Certification in Research No. 93/GCN-HĐĐĐNCYYSSH-ĐHYHN, Hanoi, 9 June 2023). Written informed consent was obtained from all participants or their legal guardians for genetic testing and publication, including images and the pedigree.

III. CASE STUDY

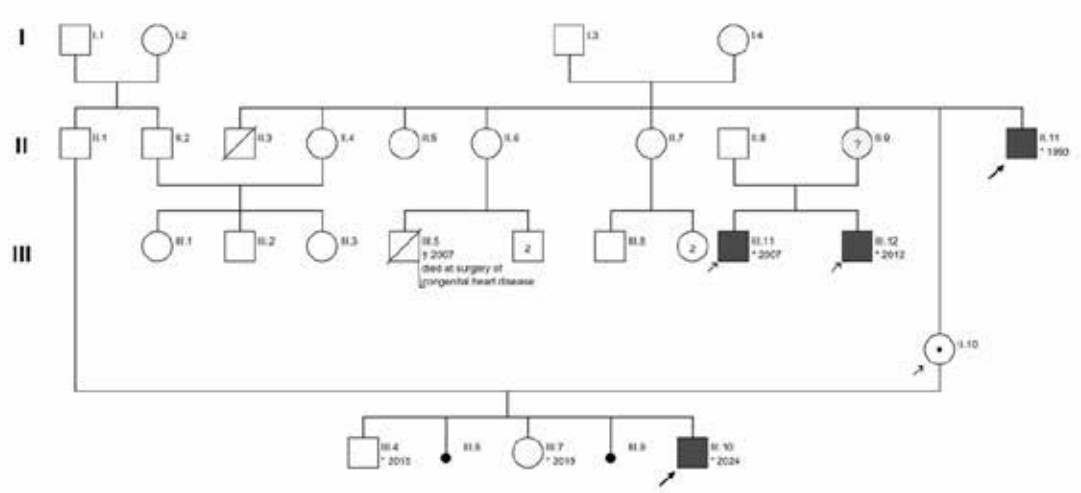

Figure 1. Family pedigree with the black arrows indicating the study subjects

Patient III.10

A 10-month-old boy was referred to the Center of Clinical Genetics and Genomics, Hanoi Medical University Hospital, for evaluation of global developmental delay and a positive family history of neurodevelopmental disorders. He was born via cesarean section at 36 weeks and 5 days of gestation due to fetal distress following a pregnancy complicated by intrauterine growth restriction. Birth weight was 2.6 kg. At 10 months old, developmental assessment showed delayed milestones, with inability to roll over and poor head control. In addition, he experienced frequent brief focal tonic spasms of both hands several times per day, each lasting a few seconds without loss of consciousness. At seven months of age, a congenital ventricular septal defect was identified and corrected by surgical intervention. He also suffered from recurrent bronchiolitis requiring repeated hospitalization.

Dysmorphic features included a tall forehead, thin tented upper lip, low nasal bridge, down slanting palpebral fissures, low-set ears and facial hypotonia.

A

B

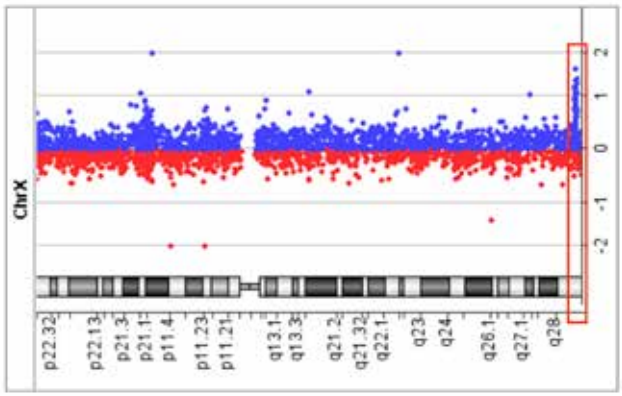

Figure 2. Facial features of patient III.10, 10 months old (A) and CMA result (B)

Table 1. CNV interpretation scoring

Evidence type	Evidence/ Criteria met	Justification	Point
Genomic Content	**1A**: Contains protein-coding or other known functionally important elements	The identified copy number variation (CNV) fully overlaps the ClinGen pathogenic region (ISCA #46304), originally curated by the International Standards for Cytogenomic Arrays (ISCA) Consortium.	0
Overlap with Established Triplosensitive (TS), Haploinsufficient (HI), or Benign Genes or Genomic Regions	**2A**: Complete overlap; the TS gene or minimal critical region is fully contained within the observed copy number gain	ClinGen Triplosensitivity (TS) Score is 3 with sufficient evidence for triplosensitivity[18]	+1
Gene Number - Number of protein-coding RefSeq genes wholly or partially included in the copy number gain	**3A:** 0-34 genes	This structural variant affects 20 coding genes: ABCD1, ARHGAP4, AVPR2, BCAP31, CCNQ, and 15 more.	0
Evidence from Public and Internal Data	**4L**: Statistically significant increase amongst observations in cases (with a consistent, specific, well-defined phenotype) compared to controls	- ClinVar entries with at least 80% reciprocal overlap variants reported as P/LP: 2 entries (#58709, #253514) - ClinVar entries with at least 50%-80% reciprocal overlap variants reported as P/LP: 14 entries (#58740, #148069, #151852...) - Decipher entries with at least 80% reciprocal overlap variants reported as P/LP: 2 entries (#322850, #284409) - Decipher entries with 50%-80% reciprocal overlap variants reported as P/LP: 7 entries (# 317935, #356374, # 324181)[19]	+0.15

Evidence type	Evidence/ Criteria met	Justification	Point
Patient inheritance pattern or family history	**5D.** CNV segregates with consistent phenotype observed in the patient's family.	Inheritance pattern concordant with reported mechanism	0.45
Total			1.60

Classification (Scoring: pathogenic 0.99 or more points, likely pathogenic 0.90 to 0.98 points, variant of uncertain significance 0.89 to −0.89 points, likely benign −0.90 to −0.98 points, benign −0.99 or fewer points): Pathogenic

Given the suspected genetic etiology, the patient III.10 underwent karyotyping, CGG repeat expansion on the *FMR1* gene for Fragile X syndrome testing, and CMA. Karyotype result and CGG expansion numbers found no abnormality (36 repeats), while CMA identified a maternally inherited duplication at chromosome Xq28. The breakpoint of the duplication position was located between 153,594,028 and 154,140,741 on X chromosome (GRCh38), spanning 546 kb, encompassing the MECP2 locus and 12 morbid genes (gene that has been conclusively associated with human disease) in OMIM (Online Mendelian Inheritance in Man) database: *ABCD1, AVPR2, BCAP31, CCNQ, HCFC1, IDH3G, L1CAM, MECP2, NAA10, SLC6A8, SRPK3, SSR4*. Based on the child's clinical manifestations and classification as Pathogenic according to the ACMG/ClinGen 2020 criteria (Supplementary Table 1),[10] a diagnosis of MDS was confirmed. Considering his positive family history and examination, CMA testing was subsequently performed for his two maternal cousins (patients III.11 and III.12).

Table 2. Summarizes the clinical features observed in our four affected probands compared with previously reported cases in the literature

	III.10	III.11	III.12	II.11	Adapted from article review by Ta et al. 2022
Sex	Male	Male	Male	Male	Mostly male, little or no symptom in female,
Age of first examination	12 months	18 years	13 years	32 years	
Age of onset	7 months	3 years	3 years	32 years	
Dysmorphic feature	a tall forehead, thin tented upper lip, low nasal bridge, downslanting palpebral fissures, low-set ears and facial hypotonia	Thick lip, wide front Narrow nasal alar	Wide front, big ears, narrow nasal alar, gapped teeth, prominent central incisors	narrow nasal alar, low nasal dorsum	Mild abnormalities: small midface, big ears, low nasal dorsum
Communication skills	Language: 6-8 months Personal-social: 7-9 months Cognitive: 9-10 months	Absent speech Able to recognized familial/ unfamilial	Absent speech Able to recognized familial/ unfamilial Incontinence	Absent speech Able to recognized familial/ unfamilial Incontinence	Absent speech (69 %) Few words/ limited speech (25%)

	III.10	III.11	III.12	II.11	Adapted from article review by Ta et al. 2022
Gross motor function	Gross motor: 6-8 months Fine motor: 5-7 months	Acquisition of walking	Acquisition of walking	Acquisition of walking	Acquisition of head control (89%) Acquisition of sitting (92%) Acquisition of walking (65%)
Regression of gross motor skills	-	-	-		Regression of gross motor skills (39%)
Neurological signs	Hypotonia	Ataxia or ataxic/wide-based gait. Spasticity. Choreiform hand movements	Ataxia or ataxic/ wide-based gait. Spasticity. Choreiform hand movements	Ataxia or ataxic/ wide-based gait. Choreiform movements	Ataxia or ataxic/ wide-based gait (58%) Spasticity (45%) Choreiform movements (63%)
Regression of purposeful hand use	-	-	-	-	Regression of purposeful hand use (21%)

	III.10	III.11	III.12	II.11	Adapted from article review by Ta et al. 2022
Epilepsy	Focal myoclonic seizure involving 2 hands, jerk every 10-15 seconds, alert, multiple seizures in a 24-hour period. Onset in post natal, in remission	Tonic seizure, onset at 10 years, 10-20 seizures per month	-	-	Seizures/ Epilepsy (53%) Treatment-refractory seizures (68%)
Behavioral disorders	-	Repetitive behavior: hands clapping and rubbing Irritability	Repetitive behavior: hands clapping and rubbing	Irritability	Either relaxed, sociable or autistic spectrum disorders, irritable
Cardiovascular system	Ventricular septal defect operated at 7 month	N/A	N/A	N/A	21 % have vascular defects
Respiratory system	Bronchiolitis in post natal (1-2 episodes per month)	Recurrent pneumonia, bronchiolitis from infant	Recurrent pneumonia, bronchiolitis from infant	Recurrent pneumonia, bronchiolitis from infant	Multiple episodes of respiratory infections

	III.10	III.11	III.12	II.11	Adapted from article review by Ta et al. 2022
Gastrointestinal	-	-	-	-	Functional issues are a major clinical problem: Constipation(72%) Drooling (70%) Swallowing difficulties (50%)
Genitourinary system	-	-	-	-	Mild abnormalities: delayed testicular migration, incomplete genital system
Muscle symptoms	-	-	-	-	Muscle weakness

Patient III.11 and III.12

Two maternal cousins of patient III.10 presented in early childhood with severe motor and mental delay; each achieved independent walking only at three to four years of age. Neurological examination revealed generalized hypertonia. In addition, stereotypical handclapping and rubbing movements had been observed. The elder brother (III.11), now 18 years old, had a more severe course and developed tonic seizures at the age of ten, occurring 10-20 times per month. The younger brother (III.12), 13 years old, did not experience seizures. Both had recurrent respiratory infections since infancy but no history of cardiac, gastrointestinal, or genitourinary abnormalities.

Shared dysmorphic features included a broad forehead, large ears, narrow nasal alae, down slanting palpebral fissures, epicanthal folds, low nasal bridge, and a long face; the younger brother (III.12) additionally had a diastema with prominent upper central incisors.

Figure 3. Facial appearance of patients III.11, 18 years old and III.12, 13 years old

CMA identified a duplication at chromosome Xq28 with the breakpoint was located between 153,594,028 and 154,325,028 on X chromosome (GRCh38), spanning 731kb, involves 29 protein-coding genes, including 14 morbid genes in OMIM database: *ABCD1, AVPR2, BCAP31, CCNQ, HCFC1, L1CAM, MECP2, NAA10, OPN1LF, OPN1MW, SLC6A8, SRPK3* and *SSR4*. This finding also confirmed the diagnosis of MDS in these patients.

Patient II.11

A similar clinical phenotype was observed in their maternal uncle (II.11, 32 years old). He presents with global developmental delay and absent speech. Although able to walk independently, he remained fully dependent in daily activities and had urinary and fecal incontinence, accompanied by marked irritability.

He also had recurrent episodes of pneumonia and bronchiolitis since childhood. Facial features included hair sparse anteriorly, a low nasal bridge.

Figure 4. Facial appearance of patient II.11, 32 years old

Given the clinical resemblance to the affected nephews, genetic testing for the familial variant is pending to confirm the diagnosis of MDS and to guide genetic counseling once the results are available.

IV. DISCUSSION

Our report represents the first documentation in Vietnam with familial MDS cases across multiple developmental stages, including prenatal, postnatal, and adolescent presentations. At the initial evaluation, the family pedigree suggested an X-linked pattern of inheritance, involving three affected male cousins and one maternal uncle. CMA then identified a duplication at Xq28 segregation within the pedigree, confirmed the diagnosis of MDS, an X-linked neurodevelopmental disorder characterized by early-onset hypotonia, severe intellectual disability, minimal or absent speech, recurrent respiratory infections, and epilepsy.

In contrast to most congenital causes of intellectual disability that follow a static developmental course, MDS demonstrates a distinctly progressive neurological trajectory. In almost reports, affected infants usually present with generalized hypotonia in the neonatal and early infancy periods, also observed in our patient III.10.[11] Over time, particularly from late childhood into adolescence, this hypotonia gradually transitions to spasticity,[12] as documented in patients III.11 and III.12 at 13 and 18 years of age, respectively. Scoliosis is the most commonly reported orthopaedic issue in 27% of MDS patients, likely caused by spasticity observed in MDS, as reported by Ta et al. 2022.[11] Such findings emphasize the motor impairment in MDS and the need for longitudinal neurological assessment and multidisciplinary supportive care throughout disease progression.

Epileptic manifestations are reported in approximately half of individuals with MECP2 duplication syndrome, with a highly variable age of onset and frequency increases with age.[11] Within the same family, onset can occur as early as 10 months, as observed in our youngest affected individual, while remaining absent even in late adolescence, as in patient III.12. Nevertheless, because epilepsy can present later in adulthood, several reports-including those by Marafi et al. (2019) and Takeguchi et al. (2021)-have documented cases of late-onset seizures in adults with *MECP2* duplication syndrome, highlighting the need for continued neurological surveillance beyond adolescence.[13,14] Reardon et al. showed a consistent progressive degenerative as behavioral problems, regular multidisciplinary follow-up and systematic monitoring for seizures and other progressive manifestations are recommended.

Among our patients with *MECP2* duplications, the start points of the duplications are consistent (153,594,028 in GRCh38),

whereas the end points vary (154,325,028 and 154,140,741 in GRCh38), given the variability in size among members of the same family. This can be explained by complex recombination mechanisms: non-allelic homologous recombination, which occurs between highly similar DNA segments, and fork stalling and template switching / microhomology-mediated break-induced replication, which involves microhomology at breakpoints and can generate duplications with heterogeneous endpoints. These mechanisms have been described in *MECP2* duplication syndrome.[16,17]

To date, no clear genotype-phenotype correlation has been established. In our series, all affected males presented with severe intellectual disability and recurrent respiratory infections. Interestingly, patient III.10 harbored a relatively small duplication encompassing fewer morbid genes, had intrauterine growth restriction detected on prenatal ultrasound, congenital heart disease and early-onset epilepsy. Notably in the level of gene, only a limited number of additional genes within the duplicated region-such as *FLNA* (associated with chronic constipation or Hirschsprung disease in MDS), *GDI1* (linked to microcephaly in MDS), or RAB39B (associated with more severe phenotypes in MDS, including Dandy-Walker malformation)-have been proposed to contribute to variability in genotype-phenotype expression in MDS.[11] None of these genes was included in the duplication observed in our patients.

Among female carriers, III.10's mother had normal cognition but dysmorphology examination found a long face with midface hypoplasia, a sign that was reported in two-thirds of patients (67/99) and is a prominent clinical feature of MDS.[11] Female carriers are generally asymptomatic due to skewed X-chromosome inactivation (XCI) but may develop subtle neuropsychiatric features-such as anxiety, depression, or compulsive behaviors-that can be overlooked during routine evaluation.[9] Unfortunately, we were unable to quantify XCI ratios to correlate them with clinical variability in this study. But identifying carrier females facilitates accurate reproductive risk assessment and prenatal or preimplantation genetic testing in the future.

Our report presents longitudinal prenatal-to-adolescent data, expanding the phenotypic spectrum of intellectual disability associated with MDS. However, it is limited by the small sample size, absence of XCI testing, pending genotype confirmation in individual II.11, and incomplete paraclinical details in some patients.

V. CONCLUSIONS

In conlusion, we illustrate typical and variable manifestations of MDS and expand the spectrum of familial transmission patterns, especially changes observed from the fetal to the neonatal and adolescent period, emphasizing the importance of early genetic evaluation. Chromosomal microarray should be performed in male infants presenting with intellectual disability, recurrent infections and epilepsy to establish an accurate diagnosis, guide clinical management, implement appropriate surveillance, and provide genetic counseling for carrier mothers.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. National Center for Biotechnology Information. PubChem Gene Summary for Gene 4204, MECP2 - methyl-CpG binding protein 2 (human). https://pubchem.ncbi.nlm.nih.gov/gene/MECP2/human. *Accessed Oct*. 10, 2025.

2. Lewis JD, Meehan RR, Henzel WJ, et al. Purification, sequence, and cellular localization of a novel chromosomal protein that binds to Methylated DNA. *Cell*. 1992; 69(6): 905-914. doi:10.1016/0092-8674(92)90610-O.

3. Bajikar SS, Anderson AG, Zhou J, et al. MeCP2 regulates Gdf11, a dosage-sensitive gene critical for neurological function. *eLife*. 12:e83806. doi:10.7554/eLife.83806.

4. Dominguez G, Wu Y, Zhou J. Epigenetic Regulation and Neurodevelopmental Disorders: From MeCP2 to the TCF20/PHF14 *Complex. Genes (Basel)*. 2024; 15(12): 1653. doi:10.3390/genes15121653.

5. Gulmez Karaca K, Brito DVC, Oliveira AMM. MeCP2: A Critical Regulator of Chromatin in Neurodevelopment and Adult Brain Function. *International Journal of Molecular Sciences*. 2019; 20(18): 4577. doi:10.3390/ijms20184577.

6. Asuncion RMD, Ramani PK. Rett Syndrome. In: StatPearls. eBook. StatPearls Publishing; 2025. Accessed October 10, 2025. http://www.ncbi.nlm.nih.gov/books/NBK482252/.

7. Kaur S, Christodoulou J. MECP2 Disorders. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, eds. GeneReviews®. eBook. University of Washington, Seattle; 1993. Accessed October 10, 2025. http://www.ncbi.nlm.nih.gov/books/NBK1497/.

8. Van Esch H. MECP2 Duplication Syndrome. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, eds. GeneReviews®. eBook. University of Washington, Seattle; 1993. Accessed September 10, 2025. http://www.ncbi.nlm.nih.gov/books/NBK1284/.

9. El Chehadeh S, Touraine R, Prieur F, et al. Xq28 duplication including MECP2 in six unreported affected females: what can we learn for diagnosis and genetic counselling? *Clin Genet*. 2017; 91(4): 576-588. doi:10.1111/cge.12898.

10. Riggs ER, Andersen EF, Cherry AM, et al. Technical standards for the interpretation and reporting of constitutional copy-number variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics (ACMG) and the Clinical Genome Resource (ClinGen). *Genet Med*. 2020; 22(2): 245-257. doi:10.1038/s41436-019-0686-8.

11. Ta D, Downs J, Baynam G, Wilson A, Richmond P, Leonard H. A brief history of MECP2 duplication syndrome: 20-years of clinical understanding. *Orphanet J Rare Dis*. 2022; 17(1): 131. doi:10.1186/s13023-022-02278-w.

12. Yon DK, Park JE, Kim SJ, Shim SH, Chae KY. A sibship with duplication of Xq28 inherited from the mother; genomic characterization and clinical outcomes. *BMC Med Genet*. 2017; 18(1): 30. doi:10.1186/s12881-017-0394-7.

13. Marafi D, Suter B, Schultz R, Glaze D, Pavlik VN, Goldman AM. Spectrum and time course of epilepsy and the associated cognitive decline in MECP2 duplication syndrome. *Neurology*. 2019; 92(2): e108-e114. doi:10.1212/WNL.0000000000006742.

14. Takeguchi R, Takahashi S, Akaba Y, et al. Early diagnosis of MECP2 duplication syndrome: Insights from a nationwide survey in Japan. *Journal of the Neurological Sciences*. 2021; 422. doi:10.1016/j.jns.2021.117321.

15. Reardon W, Donoghue V, Murphy AM, et al. Progressive cerebellar degenerative changes in the severe mental retardation syndrome caused by duplication of MECP2 and adjacent loci on Xq28. *Eur J Pediatr*. 2010; 169(8): 941-949. doi:10.1007/s00431-010-1144-4.

16. Pehlivan D, Bengtsson JD, Bajikar SS, et al. Structural variant allelic heterogeneity in MECP2 duplication syndrome provides insight into clinical severity and variability of disease expression. *Genome Med*. 2024; 16(1): 146. doi:10.1186/s13073-024-01411-7.

17. Carvalho CMB, Zhang F, Liu P, et al. Complex rearrangements in patients with duplications of MECP2 can occur by fork stalling and template switching. *Hum Mol Genet*. 2009; 18(12): 2188-2203. doi:10.1093/hmg/ddp151.

18. Clinical Genome Resource (ClinGen). Xq28 region (includes MECP2) curation results for dosage sensitivity. *ClinGen Dosage Sensitivity Map*. Accessed October 10, 2025. https://search.clinicalgenome.org/kb/gene-dosage/region/ISCA-46304.

19. University of California, Santa Cruz (UCSC) Genome Browser. Human hg38 chrX:153594028-154140741 (v488). *UCSC Genome Browser Database*. Accessed October 10, 2025. https://genome.ucsc.edu/cgi-bin/hgTracks?db=hg38&position=chrX-%3A153594028-154140741.