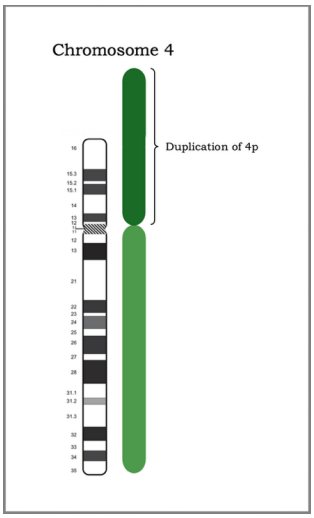
Trisomy 4p



Individuals with trisomy 4p have three copies of the short arm of chromosome 4 rather than the typical two. Those with trisomy 4p present with a recognizable group of features including developmental and intellectual delays, characteristic facial features, and occasionally congenital anomalies[2]. It should be noted that patients with "pure" trisomy 4p are relatively rare. In most known cases trisomy 4p is associated with additional imbalance due to reciprocal translocations or pericentric inversions in one of the parents, and this additional imbalance affects phenotypic manifestations[1]. The second factor influencing the clinical picture is the size of the duplicated segment: persons with trisomy for the entire 4p (or 4p12-pter, 4p13-pter) have more significant defects than persons with trisomies for the distal parts of 4p (4p15-pter, 4p16-pter).

Intellectual and developmental delays are a key feature seen in those with trisomy 4p. Some individuals may present with delayed motor milestones. For example, one individual sat unassisted at 11 months and walked without assistance at 22 months3. While developmental delays are common, some individuals are able to attend mainstream school should special support be available, while others may require special schooling altogether2,4. It is also possible for some individuals to present with various neurodevelopmental differences such as autism or hyperactivity5. It should also be noted that some with trisomy 4p may present with seizures1.

Trisomy 4p also presents with several characteristic facial features. This includes a bulbous nose, flat or depressed nasal bridge, retrognathia or micrognathia, pointed chin, short neck and low hairline, enlarged ears with a malformed helix, and microcephaly2,3.

Additionally, it is possible for some individuals to present with various congenital anomalies in the heart, kidneys, brain, or genitals1. This may include findings such as ventricular enlargement, kidney hypoplasia, or hypogonadism3,6. However, it is necessary to point out that those with trisomy of the entire 4p arm are more likely to have these congenital anomalies compared to those with only partial trisomy1.

Trisomy 4p may also cause individuals to present with abnormal hands and feet. Previous literature has shown individuals to present with rocker-bottom feet, arachnodactyly, or camptodactyly7.

REFERENCES

[1]Eid O, Eid M, Abdel Kader R, et al. (2024). Cytogenetic and Clinical Description of Maternally Inherited Pure Trisomy 4p. *Middle East J. Med. Genet*. *13*(1):16-20.

[2]Schönewolf-Greulich B, Ravn K, Hamborg-Petersen B, et al. (2013). Segregation of a 4p16.3 duplication with a characteristic appearance, macrocephaly, speech delay and mild intellectual disability in a 3-generation family. *Am J Med Genet A*. *161A*(9): 2358–2362.

[3]Liang L, Xie Y, Shen Y, et al. (2016). A Rare de novo Interstitial Duplication at 4p15.2 in a Boy with Severe Congenital Heart Defects, Limb Anomalies, Hypogonadism, and Global Developmental Delay. *Cytogenet Genome Res*. *150*(2):112–117.

[4]Varley J, Wehner T, Sisodiya S. (2015). Diaphragm myoclonus followed by generalised atonia in a patient with trisomy 4p: unusual semiology in an unusual condition. *Epileptic Disord*. *17*(4): 473–477.

[5]Polan MB, Pastore MT, Steingass K, et al. (2014). Neurodevelopmental disorders among individuals with duplication of 4p13 to 4p12 containing a GABAA receptor subunit gene cluster. *Eur J Hum Genet*. *22*(1):105–109.

[6]Demirhan O, Özgünen F, Taştemir D. (2010). Clinical Manifestations of Partial Trisomy 4p. BJMG, 13(2): 61-63.

[7]Nasri K, Ben Jamaa N, Ouertani I, et al. (2024). Partial Trisomy 4p Syndrome Diagnosed Prenatally. *Fetal Pediatr Pathol*. *43*(2):188–195.