TRISOMY 12P

Trisomy 12p

Individuals with trisomy 12p have three copies of the short arm of chromosome 12. Estimated to occur in roughly 1/50,000 births, trisomy 12p is often caused by improper segregation of a balanced parental translocation[1,2]. However, many patients have de novo (or new) abnormality not inherited from a parent[2]. Those with trisomy 12p can be classified into different sub-groups depending on the extent or region of the 12p trisomy, whether or not the trisomy is mosaic or complete, and whether or not additional chromosomal imbalances are present[3]. There may be a great deal of genetic heterogeneity and, for this reason, some phenotypic heterogeneity can be seen.

Trisomy 12p is characterized by dysmorphic features, intellectual and developmental delays, as well as the potential for certain congenital anomalies, including defects of the brain and heart. Specifically, those with trisomy 12p present with a long face, high forehead, receded anterior hairline, wide spaced eyes, short palpebral fissures, long philtrum, thin upper lip, wide mouth, and prominent chin[1]. A general flat and full cheek appearance is common[4]. These features may look similar to trisomy 21 so much so that some patients have been initially misdiagnosed has having trisomy 21 until molecular confirmation showed otherwise[2]. This misdiagnosis is also because a free additional marker chromosome including the centromere and short arm of chromosome 12 looks similar to the additional chromosome 21 (upon a “standard” cytogenetic examination).

Those with trisomy 12p also often present with developmental delays and intellectual disability that may be severe. These delays may affect cognitive, language, and social development[3]. For example, speech is often delayed with some patients speaking a few words while others are completely non verbal[1]. Motor delays for tasks such as head control and walking may also be significantly delayed with some not being able to walk independently until age four[5].

Behavioral concerns have also been reported in some patients. This may include behaviors such as self-mutilation, self-injurious, or self-stimulating behavior, aggression, mood swings, or severe sleep disturbances[1]. Others, however, are reported to have a generally friendly and cheerful demeanor[5].

Lastly, a variety of other anomalies may be present in those with trisomy 12p. Neurologically, hypotonia, hypertonia, and seizures may be seen[1]. The type and frequency of seizures may vary[4], but it has been reported that they generally begin around the ages of seven or eight – although have been reported to be present in children as young as one[2].

Early in the neonatal period, complications including poor feeding, cyanosis, hypothermia, hypoglycemia, hypothermia, hyperbilirubinemia and pulmonary hypertension have all been previously seen[1]. Additionally, some individuals may also present with defects of the corpus callosum and usually mild heart defects (although at least one patient had a hypoplastic left heart[6]).

Patients with mosaic trisomy 12p may have hypopigmented skin areas on the trunk and extremities.

Of note, trisomy 12p is often reported as Pallister-Killian syndrome (PKS). However, Pallister-Killian syndrome is a separate syndrome of its own categorized by tetrasomy 12p and is often in a mosaic form[2]. There may be phenotypic overlap between PKS and trisomy 12p, but they are separate conditions.

REFERENCES

[1]Segel R, Peter I, Demmer LA, et al. (2006). The natural history of trisomy 12p. *Am J Med Genet A*. *140*(7): 695–703.

[2]Oliveira JS, Joaquim TM, Silva RABD, et al. (2020). Non-mosaic partial duplication 12p in a patient with dysmorphic characteristics and developmental delay. *Genet Mol Biol*. *43*(1): e20180285.

[3]Eid MM, Helal SI, Meguid NA. et al. (2014) Nonmosaic partial duplication 12p: clinical and cytogenetic findings and review of the literature 12p duplication: clinical and cytogenetic description. *Med Res J*. 13:68-73.

[4]Arghir A, Popescu R, Resmerita I, et al. (2021). Pallister-Killian Syndrome versus trisomy 12p - a clinical study of 5 new cases and a literature review. *Genes (Basel)*. *12*(6): 811.

[5]Lim EC, Ng, IS, Yong, MH, et al. (2013). De novo trisomy 12p in twin girls with different levels of mosaicism. *Am J Med Genet A*. *161A*(7): 1702–1705.

[6]Gang MH, Lee YW, Lim HH. et al. (2019) Trisomy 12p syndrome secondary to a balanced maternal translocation [46,XX,t(12;22)(p11.2;p13)]. *Korean J Perinatol*. 30(4):254-259.