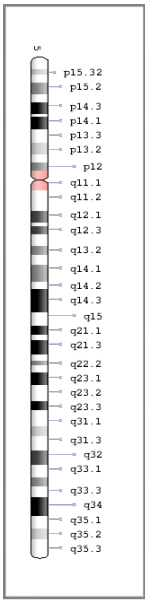
5q35 Duplication

Segment q35 on the long arm of chromosome 5, when deleted, causes Sotos syndrome. Individuals with Sotos syndrome are characterized by overgrowth, accelerated bone age, and learning difficulties. Interestingly, when this same region is duplicated rather than deleted, a "reverse Sotos" syndrome is present[1]. Characterized by short stature, microcephaly, developmental delays, and various congenital anomalies, 5q35 microduplications result in what appears to be the opposite of Sotos syndrome[2].



Within the 5q35 region exists a gene called NSD1. NSD1 is expressed in all tissues, but is mostly expressed in the brain, endocrine tissues, and reproductive organs. The resulting protein functions to regulate the expression of other genes in the same tissues[3].

When NSD1, or the 5q35 region, is duplicated, 5q35 duplication syndrome is the result. As mentioned, there are several key features identified in individuals with this duplication. One of the most commonly seen is an overall short stature and growth restriction both prenatally and postnatally[1]. Childhood weight and height in these individuals can range from below average to severely restricted[4]. In addition to the patient's overall small stature, 80% are identified to have microcephaly or low occipitofrontal head circumference[1].

5q35 duplication syndrome may also result in an individual having developmental delays, intellectual disability, and an increased risk for various psychiatric and behavioral concerns. Motor delays are present in around 63% of individuals and mild to severe intellectual disabilities are present in up to 73%[1]. More specifically, children have been identified to have delays in adaptive, receptive, expressive, fine and gross motor skills. As a result, children may require special classes in school[3]. Patients may experience mood swings, aggression, depression, psychosis, poor sociability, oppositional behavior, or attention deficit with or without hyperactivity. Some of these behavioral

disturbances may be severe enough to affect an individual's ability to perform in their job or require hospitalization[3].

While less common, individuals with 5q35 duplication syndrome can also present with various congenital anomalies. Affected systems can include cardiac, gastrointestinal, renal and uro-genital[2]. Identified cardiac defects included hypoplastic left heart, atrial septal defect, and ventricular septal defect[4] while previously identified gastrointestinal defects included imperforate anus and anorectal fistula[3].

There have also been several digital anomalies identified in individuals. For example, syndactyly, polydactyly, absent thumbs and brachydactyly can all be seen[4]. Additionally, in contrast to Sotos syndrome, individuals with 5q35 duplications may present with delayed bone age rather than matured bone age[1].

There are some characteristic facial features that may also be present in individuals with 5q35 duplication syndrome. Epicanthal folds, telecanthus, periorbital fullness, palpebral fissure, hyper/hypotelorism, strabismus, almond shaped eyes, wide nasal bridge, prominent nasal tip, long nose, flat philtrum, thin upper lip, down turned mouth, and micrognathia have all been previously described[3].

It should be noted that the patients with relatively mild manifestations of this condition may have their own children with a 50% chance to transmit this duplication[2-4]. Therefore, cytogenetic examination of the parents having a child with 5q35 duplication is a necessary step for genetic counseling in these families.

REFERENCES

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