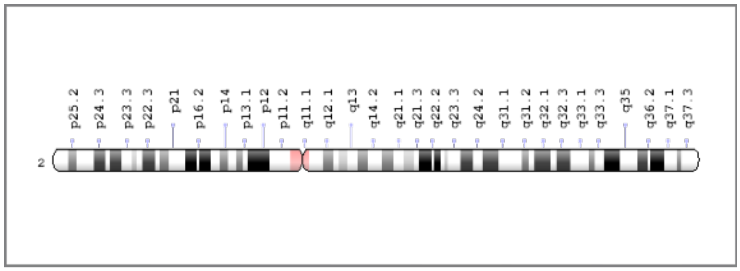
2Q33 DELETION

2q33 Deletion

The chromosomal segment 2q33 includes several genes. One of these genes – SATB2 is a key transcription factor that aids in neural development and activates several other genes simultaneously. When it is absent, cortico-cortical neurons cannot be specified and axons cannot cross the corpus callosum[1].

Defects in this gene cause the SATB2-associated syndrome which is generally characterized by developmental and intellectual disabilities, behavioral issues, delayed growth, and craniofacial abnormalities.



SATB2 associated syndrome may be caused both by mutations in the SATB2 gene and by deletions encompassing this gene (or at least part of this gene)[2]. The patients with deletions of this gene contribute to ~20% of the whole pool of persons with SATB2 associated syndrome[2]. So far more than 50 persons with deletions 2q33 involving SATB2 gene have been reported. Size of the deletions varies from 600 kb to 26 Mb. Approximately 1/3 of individuals had deletions greater than 15 Mb. All deletions are sporadic.

Developmental and intellectual delays are seen in all patients with 2q33 deletions. This includes things like delayed developmental milestones - specifically speech. Individuals with 2q33 deletions are often have limited or absent speech. In 69% of individuals ages 4 and older, speech was limited to 10 words or less[2]. Speech ability was not correlated with the deletion size. Other key milestones, such as walking, can also be significantly delayed with some children taking as long as 32 months to begin walking on their own[3]. Autism spectrum disorders have also been associated with individuals containing this deletion.

There are several key dysmorphic features of patients with 2q33 deletions. Individuals tend to have palatal and dental abnormalities; cleft palate is found in 50% of patients[2]. Dental abnormalities include microdontia, especially for upper central incisors. Relative microcephaly is also very common. Other facial phenotypes include down slanting palpebral fissures, prominent nasal bridge and low set ears[4]. Patients also have increased risk for heart defects[1] which are found in a quarter of patients. These defects are usually not life-threatening and include persistent ductus arteriosus, septal defects or defects of cardiac valves.

Patients with 2q33 deletions also tend to have delayed growth and failure to thrive. This is in part due to eating issues (80%). As a result, many (24%) are required to be fed through a gastrostomy tube or nasogastric feeding. Almost half of individuals with this deletion are characterized as underweight for their age and short for their stature[2].

Another key feature of 2q33 deletions are abnormal behaviors. Individuals tend to have a specific behavior pattern that includes hyperactivity, motor restlessness, and chaotic behavior. Patients tend to have a happy personality and demeanor overall but may have spouts of aggression, sleeping problems, anxiety, and self-mutilation. These problems can be managed through antipsychotic medication should they be dominated by self-mutilation and aggression[5].

Comparison of basic clinical findings in patients with deletions and mutations of the SATB2 gene showed similar frequency for most clinical manifestations in both groups. The only difference was regarding growth retardation: patients with deletions show more significant growth delay, and difference between real growth and normal growth for the given age increases in older children[2].

Relatively large deletions in some patients may also involve genes COL3A1 and COL5A2 located relatively close to 2q33. Patients with such deletions may reveal aortic dilation, thin and lightly bruising skin.

Individuals that have early neurodevelopmental delays, severely absent speech, and have palatal and dental abnormalities are recommended to be screened for 2q33 deletions. A majority of patients with 2q33 are diagnosed with a comprehensive neurodevelopmental evaluation. This may or may not include a brain MRI to look for any anomalies[1].

REFERENCES

[1]Zarate, Y.A., Fish, J.L. SATB2-associated syndrome: Mechanisms, phenotype, and practical recommendations. Am J Med Genet A. 2017, v. 173:327-337.

[2]Zarate, Y.A., Bosanko, K.A., Thomas, M.A., et. al. Growth, development, and phenotypic spectrum of individuals with deletions of 2q33.1 involving SATB2. Clin Genet. 2021, v. 99:547-557.

[3]Yu, N., Shin, S., Lee, K.A. First Korean case of SATB2-associated 2q32-q33 microdeletion syndrome. Ann Lab Med. 2015, v. 35:275-8.

[4]Balasubramanian, M., Smith, K., Basel-Vanagaite, L., et. al. Case series: 2q33.1 microdeletion syndrome--further delineation of the phenotype. J Med Genet. 2011, v. 48:290-8.

[5]Gregoric Kumperscak, H., Krgovic, D., Vokac, N.K. Specific behavioural phenotype and secondary cognitive decline as a result of an 8.6 Mb deletion of 2q32.2q33.1. J Int Med Res. 2016, v. 44:395-402.