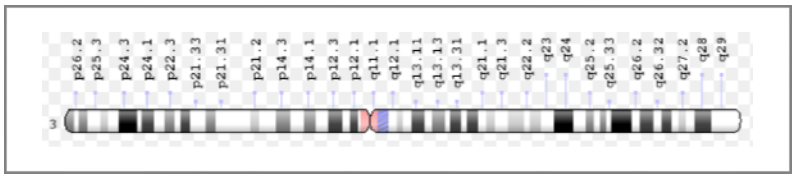
# 3Q29 DELETION

## 3q29 Deletion




The segment 3q29 is a terminal portion of the long arm of chromosome 3. Hemizygous deletions of this segment occur relatively frequently; several hundred individuals with this deletion have been reported so far. Most patients have a "standard" 1.6 Mb deletion. In most cases, deletions occur de novo but there are reports of 3q29 deletion being inherited from a mildly affected or apparently healthy parent. Most patients are diagnosed after 1-2 years of age because as a rule there are no reasons for cytogenetic examinations at an earlier age[1].

This deletion and its corresponding manifestations were first reported in the early 2000s. As of late, it is estimated that 1:30,000-40,000 individuals are affected[2].

The key clinical manifestations specific to this deletion include a complex neuropsychiatric profile, intellectual disability, growth delay, and dysmorphic physical traits.

There is a wide range of neuropsychiatric phenotypes for individuals with a 3q29 deletion. About a quarter of individuals will have a psychiatric disorder, and the burden of these disorders can be substantial for patients and their families[3]. This includes disorders such as schizophrenia, psychosis, bipolar disorder, depression, anxiety, phobias, oppositional defiant disorder, and panic attacks. Individuals also have an increased chance of an autism spectrum diagnosis in comparison to those without the deletion[4]. Attention deficit hyperactivity disorder (ADHD) is also very common (63%) among individuals with the deletion[5]. Autism may be found in 38% of affected individuals.

At least 30% of individuals with the 3q29 deletion have intellectual disability usually ranging anywhere from mild to moderate but ~5% have significant

developmental delay. In most other affected persons IQ is at the lower part of normal values. Intellectual disability may be associated with autism spectrum disorder or social/communication impairment[4]. This often results in many patients having a learning disability (92%) and requires them to receive some level of special education services while in school. However, some may not require academic support[1].

Growth delays are seen early on in life for patients with the deletion. During the first year of life, many (64%) will have elevated feeding problems. This may be presented as having severe food selectivity or food refusal. Many will meet the necessary criteria for an avoidant and restrictive food intake disorder (ARFID). The lack of nutrients may result in faltered growth as well as exacerbation of neurodevelopmental concerns. Patients may require oral nutritional supplementation or a feeding tube to support growth. Patients often have a failure to thrive[2]. The overall growth parameters for patients are lower than average for their expected age and sex[5].

There are several dysmorphic features that go along with having a 3q29 deletion. This includes long and narrow faces with a short philtrum and high nasal bridge, gait abnormalities, chest deformities, long tapering fingers, microcephaly, cleft lip/palate, horseshoe kidney/hypospadias, laxity of ligaments, and abnormal pigmentation[4]. Individuals may also have recurrent middle ear infections and various eye diagnoses including strabismus, astigmatism, and myopia[5]. It should be noted however that patients with unusual manifestations (as cleft lip/palate or horseshoe kidney) may be preferentially reported, and analysis of publications may give a skewed clinical picture.

Individuals who have been diagnosed with a 3q29 deletion should go through various screenings for neurodevelopmental and psychiatric disorders at multiple points across their lifespan. It is possible for various psychiatric disorders to present themselves at later points in life.

It is important to note that many of the more severe cases of a 3q29 deletion are the ones being reported in literature. As tests for physical traits, cognitive ability and psychiatric illness are evolving and becoming more specific, family members related to those with a severe phenotype of 3q29 (i.e. parents) are also being diagnosed with the same deletion. However, these family members are seemingly unaffected or only mildly so[3]. As time and testing progress, it may result in a reevaluation of what criteria are necessary for a 3q29 deletion diagnosis.

To obtain unbiased information about manifestations of 3q29 deletion and to optimize methods of treatment there is the “Emory 3q29 Project” at Emory University (Atlanta, Georgia).

There are other forms of 3q29 deletion which may affect other areas of 3q29 (and other genes). Deletion of the gene RPL35A located at the distal end of 3q29 (and usually not involved in persons with the typical 3q29 deletion) causes the so-called Diamond-Blackfan anemia (aplasia of the red blood cells in

association with some malformations and growth delay)[6]. The patients with deletions (or mutations) of the RPL35A are predisposed to development of different tumors.

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