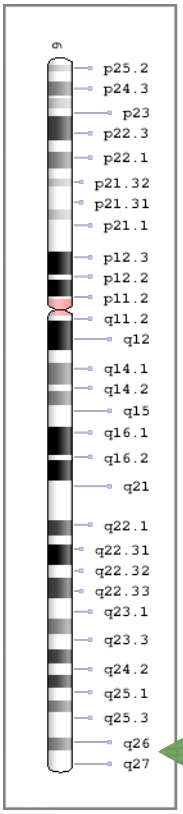
Deletions 6q26-6q27



Bands 6q26 and 6q27 are the most distal segments of the long arm of chromosome 6. Many patients have been identified as having deletions in this area. Isolated deletions of 6q26 are interstitial, while deletions involving 6q27 are mostly terminal. A majority of these deletions occur de novo, but a significant percentage of patients reveal deletions either directly inherited from healthy (or mildly affected) parents or caused by balanced rearrangements (translocations or inversions) in one of the parents[1].

The size of the segment 6q26 is ~4 Mb, and at least half of this segment is occupied by two genes: PRKN and its activator PACRG. Almost all known isolated 6q26 deletions affect at least one of these genes. The most common findings in patients with such deletions are autism and epilepsy. These manifestations may occur in patients that have total deletions of these genes or in patients with relatively small deletions of segments (exons) within the PARK gene[2]. In this situation, the size of the deletion is not directly correlated with the severity of the condition. At the same time, intellectual development of patients with isolated 6q26 deletions is usually normal. Patients with these deletions can also have significant clinical variability. For example, in several families, the same deletion was found in a proband with autism and/or epilepsy and in one of his/her unaffected parents. It should be mentioned that structural defects of the brain or other organs are not typical characteristics of isolated deletions 6q26[2].

The situation is different when the band 6q27 is also involved. These patients reveal developmental delays and intellectual disabilities, structural brain anomalies, dysmorphic features, and seizures.

As previously mentioned, phenotypes can have a wide range of expression among affected individuals. This is particularly true for developmental delays and intellectual disabilities. Those who have the most severe developmental and intellectual delays will have several major milestone delays. This includes skills like sitting independently, crawling, and walking. About half of patients with such deletions have some form of seizures[1].

Structural brain anomalies are typical for patients with 6q deletions involving 6q27. The most common defects are cerebellar hypoplasia (86%), enlarged brain ventricles (82%), corpus callosum abnormalities (68%), and gyration abnormalities (41%)[3]. Other neurological anomalies not as frequently found in patients include hydrocephalus (27%) and spinal cord malformations (22%)[4]. It has been shown that structural brain defects are caused by deletion of the DLL1 gene, located at the distal tip of 6q27[3]. Even point mutations, rather than full deletions, of this gene can cause the same spectrum of brain defects. As a result, people with even tiny terminal 6q deletions (as well as most individuals with ring chromosome 6) may reveal a wide spectrum of brain abnormalities. Structural defects of other systems (heart, kidneys, gastro-intestinal tract) are uncommon.

Terminal 6q deletions may also cause a spectrum of dysmorphic features. A broad nasal tip, prominent nasal bridge, thin lips, low-set ears, retrognathism, and a short neck are all reported features found in patients[3]. These dysmorphic features can be seen in all stages of life, with some being identified prenatally[1].

This deletion may be identified and diagnosed at any stage of life. About 25% of cases have been identified prenatally, while most other cases have been identified during infancy and childhood. A minority of cases have been identified when the patient was an adult[1]. This range in age at diagnosis only further emphasizes the broad range of possible phenotypes in patients.

REFERENCES

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