DELETION 1P31.3

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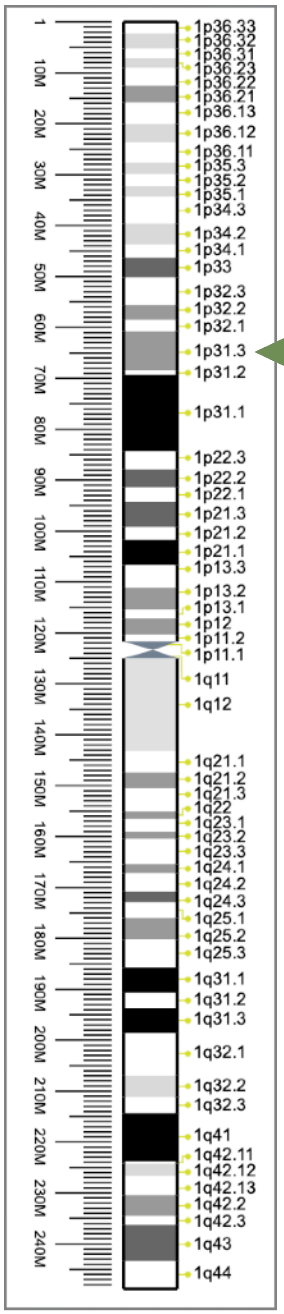
The most known condition caused by deletion of the short arm of chromosome 1 is deletion 1p36. However, recent studies show that several more syndromes may be attributed to deletions of other segments of 1p. One of these conditions is deletion of the 1p31.3 segment. This segment includes the NFIA gene located at 60.865-61.463 Mb. NFIA is an important transcription factor whose main function is facilitating various differentiation pathways during embryogenesis[1]. It has been shown that those who have mutations or deletion in this gene, resulting in haploinsufficiency, causes a syndrome mainly characterized by central nervous system malformation, facial dysmorphisms, and urinary tract defects[2,3].



At least 40 cases involving deletion of this area have been reported so far. Most cases of these deletions are reported to be de novo. However, the few cases that have been shown to be inherited from a parent are passed on in an autosomal dominant fashion[4]. Some deletions affect only NFIA gene whereas in other cases many other genes seem to be involved.

Most individuals with chromosomal deletion 1p31.3 have abnormalities in their central nervous system, intellectual disabilities, developmental delays,

neuro-psychological problems, urinary tract defects, and some dysmorphic facial and bodily features.

Morphological defects of the brain and skull are the cornerstones of this condition. The most common defects are agenesis or hypoplasia of the corpus callosum which was found in 22 out of 38 informative cases. Craniosynostosis (premature closure of sutures between cranial bones) was reported in 13 cases (extremely high frequency compared to other chromosomal syndromes). Relatively frequent defects include macrocephaly (10) or hydrocephalus (4). Other defects include polymicrogyria, cerebellar defects, Chiari type I malformation or tethered spinal cord[5]. At least two patients had extremely rare Moyamoya disease – stenosis of arteries in the area of the basal ganglia.

Patients with 1p31.3 deletions also reveal intellectual disabilities, developmental delays, and behavior abnormalities. These disabilities and delays can range from mild to severe. Developmental delays can include delays in milestones such as crawling, sitting, walking, or other motor skills[3]. Neurological abnormalities can include bipolar disorder, depression, attention deficit hyperactivity disorder, obsessive compulsive disorder, and autism spectrum disorder[4]. Seizures have been reports at least in 5 patients.

Defects of the urinary system also are relatively common; they have been reported at least in 9 patients. These abnormalities include hydronephrosis, hypoplastic or ectopic kidneys. However most of these defects do not lead to renal insufficiency.

Defects of extremities are common but relatively mild (shortening of the limbs, proximally placed thumbs, camptodactyly etc.). Whereas dysmorphic facial features (high forehead, ptosis, low-set ears etc) are reported at least in 50% of patients.

All these defects are direct result of deletion of the NFIA gene because they present even in patients who did not lose any other genes.

At the same time, all 6 cases of congenital heart disease were reported in patients having associated deletions of other neighboring genes. Most likely, heart defects are not features of deletion 1p31.3 per se.

It should be noted that point mutations within the NFIA gene cause basically the same manifestations as deletions.

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