DELETION 10Q26

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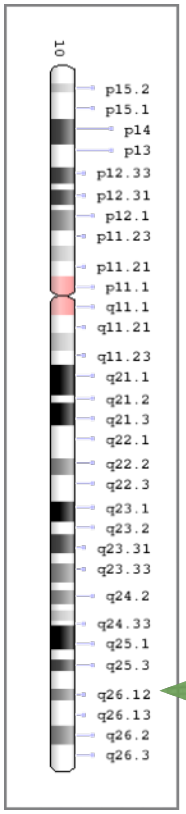

10q26 is the most distal segment on the long arm of chromosome 10. This segment is relatively large, with its size being ~16 Mb. There are numerous reports of patients having deletions in this area, with the first publications regarding this deletion having appeared in 1978[1]. Some deletions are terminal, while others are interstitial. Almost all interstitial deletions are sporadic. A significant proportion of terminal deletions are caused by reciprocal translocations or pericentric inversions in one of the parents. Virtually all patients of this group have an associated imbalance for other chromosomal areas. Only "pure" cases of 10q26 deletions were used for the analysis of the phenotype.

It should be noted that 10q26 deletions do not constitute a clinically recognizable condition since it may be explained by both deletions of different areas within 10q26 and by clinical variability, even in patients with virtually identical chromosomal imbalance.

There have been attempts to identify a critical region among patients, where a specific deletion causes most if not all identified phenotypes, but no single region has been identified. There have even been individuals identified who do not have any portion of their deletion overlapping with proposed critical regions, yet they still manifest similar phenotypes[2]. Some symptoms common for patients with 10q26 deletions are similar to manifestations in patients with other forms of a chromosomal imbalance.

Individuals with 10q26 deletions reveal a variety of clinical features. This includes growth delays, intellectual disabilities and developmental delays, craniofacial dysmorphism, and defects of the internal organs.

The growth delay common for this condition tends to manifest prenatally as intrauterine growth retardation. These delays in growth can often be seen in utero and can be detected when receiving an ultrasound during pregnancy[3]. The slow growth can continue postnatally and cause a short stature to develop later on in life[4].

Intellectual disabilities and developmental delays are also common in patients with 10q26 deletions, but not all individuals are the same when it comes to these disabilities and delays. However, some form of developmental delay is reported in 89% of patients[5]. Developmental delays can be seen by a delayed motor ability. Some children are unable to roll over, sit, or crawl on their own as late as 8 months of age. Some patients may also have difficulties speaking and will require some form of speech therapy[3]. Some authors include ataxia in the list of clinical manifestations[4]. Cherik et al.[6] suggest that the loss of the INSYN2 and NPS genes may be responsible for cognitive problems in patients

with deletions involving the subsegment 10q26.2, but that similar cognitive dysfunction may be found even in patients in whom these genes were not deleted. Of course, a 16 Mb segment of DNA may contain many genes involved in neurogenesis.

10q26 deletions also cause craniofacial dysmorphism in a patient. It is shown that around 70% of individuals with the deletion will have some form of craniofacial dysmorphism. This can include a narrow face, down-slanting palpebral fissures, high forehead with temporal retraction, micrognathia, long and flat philtrum with a thin vermillion of the upper lip[6].

Many patients with this deletion also have defects of the heart, urogenital and gastro-intestinal systems. Congenital heart defects (mostly septal defects or patent ductus arteriosus) were reported in 30% of patients (63/219). In most cases, these defects do not cause serious problems and do not require surgical correction.

Defects of the urinary system are relatively common (40/219). Most patients reveal hydronephrosis, dilated ureters or vesicoureteral

reflux. At the same time, renal agenesis or cystic renal dysplasia are highly unusual. Several patients have hypoplastic or even ambiguous genitalia. Comparative analysis of patients with different deletions shows that genes responsible for genitourinary defects should be located at subsegments 10q26.12-10q26.13[3].

Gastro-intestinal abnormalities include anal abnormalities (8/219) and esophageal or duodenal atresia. It should be noted that not a single patient with deletions of the most distal 7 Mb of 10q26 had anal defects. Therefore, the gene(s) responsible for this defect should be located in more proximal areas of 10q26.

Hearing impairment seems to be relatively frequent (20/219) and may be even more common than originally thought due to many patients (especially newborn babies) have not been tested.

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