DELETIONS 8P11

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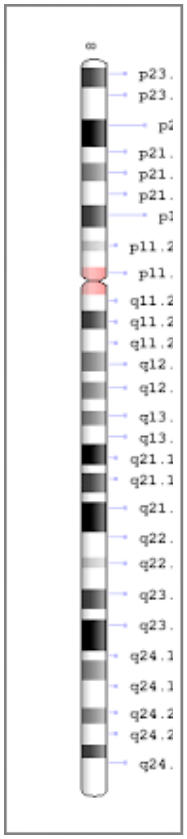

Segment 8p11 is the area of the short arm of chromosome 8 closest to the centromere. This segment includes at least 3 clinically important genes: SLC20A2, ANK1, and FGFR1. Each of these genes has their own separate functions and is causal of specific clinical features. Deletions of this area may include all 3 genes, combinations of two (SLC20A2 and ANK1, or ANK1 and FGFR1) or any single gene. Deletions of several different genes when each of these genes has its own consequences is referred to as a contiguous deletion syndrome, meaning the clinical features in patients will differ depending on which genes are deleted.

Individuals who have deletions including SLC20A2 have calcification of the basal ganglia. This cerebral microvascular calcification is associated with several other neuropsychiatric conditions. Neuropsychiatric conditions can include parkinsonism, tremors, dystonia, cognitive impairment, psychiatric problems, and ataxia. Some patients, however, can remain asymptomatic for these neuropsychiatric disorders[1]. Additionally, patients whose deletions include SLC20A2 may also have a variety of other speech and cognitive abnormalities[2].

ANK1, the next important gene in 8p11 deletions, causes hereditary spherocytosis. Spherocytosis is one of the most common hemolytic anemias[3] and is caused by red blood cells being unable to maintain their typical biconcave shape. This then results in anemia, splenomegaly, and premature destruction of the blood cells[4]. Individuals whose deletions included ANK1 have also been seen to

have growth retardation, microcephaly, developmental delay, and distinctive facial features[4].

The third important gene in 8p11 deletions is FGFR1. Deletion of FGFR1 results in Kallmann syndrome which is characterized by anosmia (lack of sense of smell), hypogonadism (micropenis, hypoplastic scrotum, cryptorchism) as well as abnormal hormonal levels (low levels of luteinizing hormone and follicle stimulating hormone[5]). Kallmann syndrome occurs (or is at least being diagnosed) in males more frequently that in females. It should be noted that Kallmann syndrome is a genetically heterogeneous condition and may be also caused by mutations of deletions of other genes.

Size of deletions may be different in different persons. Patients whose deletions are relatively large can encompass more than one of these three genes and will thus have the clinical features associated with each individual deletion. For example, individuals who have a deletion in ANK1 and FGFR1 would have both spherocytosis and Kallmann syndrome.

Dysmorphic features have been reported for patients with varying sizes of 8p11 deletions, although there is a wide range as to what an individual might have. Unilateral cleft lip/palate, exophthalmos, broad nasal root, bulging forehead, convergent strabismus, thinning hair[5], crumbled ears, and micrognathia[3] have all been previously reported.

REFERENCES

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