7P21 DELETION AND SAETHRE-CHOTZEN SYNDROME

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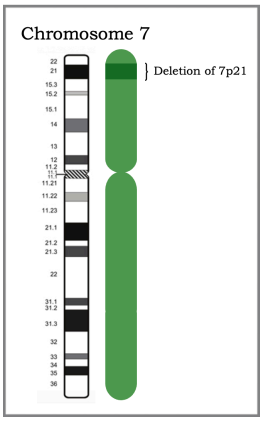

Saethre-Chotzen syndrome (SCS) is a rare disorder, affecting between 1/25,000-1/50,000 individuals. It is characterized by single or multisuture craniosynostosis, skull anomalies, dysmorphic facial features and various limb abnormalities[1]. In most cases SCS is caused by mutations of the TWIST1 gene located within the 7p21 region. However, there is a group of patients with deletions of 7p21 (involving TWIST1 gene) who also reveal manifestations of SCS.

TWIST1 is a highly conserved transcription factor that regulates osteoblast differentiation during development[2]. Osteoblast differentiation is important in skull development, and a deletion of TWIST1 alters the ossification process, resulting in abnormal suture closing[3].

Craniosynostosis is the premature fusion of cranial sutures in the skull. When this occurs, an individual's skull shape can be visibly altered at birth[1]. Bilateral coronal craniosynosis is the most common form in those with SCS (59-74%)[1]. However, unilateral coronal craniosynsosis (23%) and additional suture involvement can also be seen (21%)[1]. This process of premature fusion typically begins within the first 12 months of life[4].

Individuals with SCS may have an altered skull and facial shape due to the premature closure of these sutures. Individuals may present with trigonocephaly, plagiocephaly, lower jaw prognathism, large anterior fontanelle, facial asymmetry,

low set ears, prominent nasal bridge, beaked shape of the nose, hypertelorism, and ptosis[4,5,6]. Additionally, a low-set hairline and cleft palate can also be seen[1].

SCS can also present with various limb abnormalities including brachydactyly, syndactyly, clinodactyly, and bifid distal phalanx[4,5].

It has been seen that individuals who have SCS due to a chromosomal deletion, such a 7p21, are more likely to have developmental or intellectual delays as well as multiple medical complications than those who have mutations isolated to the TWIST1 gene[1]. The intellectual disabilities caused by 7p21 deletions are often severe[4,6].

Not all individuals with 7p21 deletions will have the same clinical features. However, it is expected that all individuals with 7p21 deletions or TWIST1 mutations will have some degree of symptoms present[1].

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