10Q24 DUPLICATION SYNDROME

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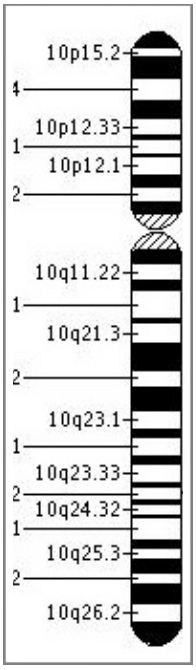

Duplication of the q24 segment on the long arm of chromosome 10 causes a relatively rare type of limb malformation called ectrodactyly. Although rare when looking at all chromosomal disorders, ectrodactyly is quite common in individuals with duplications of 10q24. Ectrodactyly, also called split-hand/foot malformation (SHFM), is present when there is a failure to maintain the central portion of the apical ectodermal ridge within the developing embryo1. As a result, there may be a complete absence or underdevelopment of the central digits and the presence of only a single phalanx2. Variable fusion of any remaining fingers and median clefts of the hands/feet are the result3. Clinically, individuals will present with features like monodactyly, syndactyly or polydactyly4.

Individuals with 10q24 duplications may have what is called SHFM type 3 (SHFM3). SHFM3 accounts for roughly 20% of all SHFM cases3. A defining feature of this type of ectrodactyly is that there is preaxial involvement within the upper limbs. While this finding may be found in other types of SHFM, it is most frequently observed in individuals with SHFM32.

It is important to note that individuals with 10q24 duplications may not have the exact same clinical features as one another. SHFM3 has both reduced penetrance and variable expression, meaning that even within the same family, there will be variability in terms of clinical features2. Additionally, this variability can exist within a single patient. Not all limbs will be affected in the exact same way5.

Additional systematic features can sometimes be identified in those with 10q24 duplications. This may include learning difficulties, intellectual disabilities, dental anomalies, and other skeletal anomalies. However, these additional findings are highly variable and are not always consistently seen among patients2.

10q24 is a relatively large segment of DNA (> 8 MB), but all duplications leading to ectrodactyly are limited to relatively small 0.5 Mb area within 10q24.3. There are several genes which may play a part in the development of the SHFM3 clinical phenotype. TLX1, LBX1, BTRC, POLL, and DPCD are all genes present within this region and are thought to potentially play a role in the development of ectrodactyly. As of late, it appears that the BTRC gene is the largest contributor to the development of clinical features3. However, the exact mechanism of how this duplication results in SHFM3 is unclear4.

Duplications of more proximal segments of 10q24 (not involving the critical 102.9-103.4 Mb area) do not constitute any recognizable phenotype.

Surprisingly large (> 10 Mb) duplications involving 10q24q25 (usually with associated deletions for other chromosomes) do not produce ectrodactyly. This may imply the existence of some regulatory elements preventing effects of “ectrodactyly-related” genes.

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