DELETION 15Q11.2

(Burnside-Butler Syndrome)

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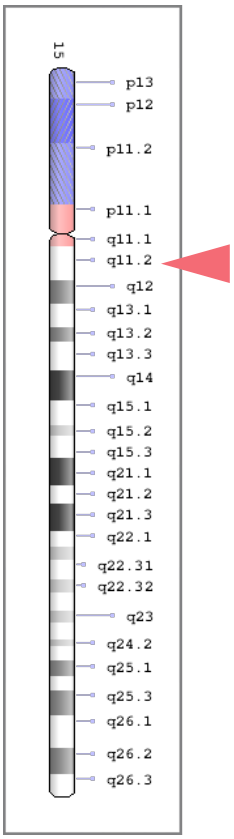

Deletions (as well as duplications) of the proximal segment of the long arm of chromosome 15 are relatively common. However, almost all breakpoints (BP) in this area are not random, but concentrated in several spots. Each of these spots has a specific position. BP1 is the closest to the centromere, more distal breakpoints are designated as BP2, BP3, etc. Burnside-Butler syndrome is a condition caused by deletions of the most proximal segment (BP1-BP2) of 15q11.2. Only four genes NIPA1, NIPA2, CYFIP1, and TUBGCP5 "reside" between BP1 and BP2.

Although each of these genes has different functions, their combined deletion results in the appearance of neurodevelopmental disorders. Together, these genes have been associated with many neurodevelopmental disorders[1]. Burnside-Butler syndrome as a whole is also becoming one of the most frequent cytogenetic findings in individuals with either autism spectrum disorder or a neurodevelopmental disorder[2]. Just downstream of this location are the regions where, if deleted, are responsible for both Angelman Syndrome and Prader-Willi Syndrome, which have similar neurodevelopmental effects[2].

Although characterized by the presence of developmental delay or autism spectrum disorder, patients with Burnside-Butler Syndrome can also present with various neurologic or behavior problems, seizures, and dysmorphic features.

A wide range of developmental delays may exist among Burnside-Butler patients. This can include both speech (90%) and motor (36%) delays. General developmental delays were seen in 59% of persons and are defined by the child being incredibly delayed in attaining certain developmental milestones[3]. A significant number of patients may also have autism or features of autism (43%)[3].

In addition to developmental delays, neurologic and behavior problems are relatively common among patients. Around 36% of patients had attention deficit disorder or attention deficit hyperactivity disorder. Additionally, 64% of patients had abnormal behavior or a neurologic problem such as obsessive compulsive disorder, tantrums, sleep problems, or an abnormal brain MRI or EEG[3]. Psychiatric problems like schizophrenia or paranoia psychosis have also been reported in some patients[4]. Seizures (21%) have also been frequently reported among individuals with Burnside-Butler syndrome[3].

The patients with Burnside-Butler syndrome may also reveal various dysmorphic features. Dysmorphic features are noted in about half of identified patients, but there are no consistent physical abnormalities[3]. Features that have been noted include broad, round face, ptosis, soft, fleshy or overfolded ears, smooth upper lip and philtrum. Other defects may include mild scoliosis and kyphosis, and both hyperextensibility and instability of various joints[3]. Serious structural defects of the brain or internal organs in patients with Burnside-Butler syndrome are exceptionally rare. Most likely that these defects are not causally related to 15q11.2 microdeletion but are just random findings in patients with this deletion.

It should be noted that a significant proportion of patients with Burnside-Butler syndrome inherited the deletion from one of their parents. Some of these parents seem to be unaffected. It may reflect a wide clinical continuum of the deletion – from apparently normal to severe neurodevelopmental problems. The presence of other genetic factors predisposing to severe manifestations (or, vice versa, protecting from such manifestations) may be another opportunity.

REFERENCES

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