Pitt-Hopkins Syndrome

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Characteristics

Pitt-Hopkins syndrome is characterized by mental retardation, a wide mouth, and intermittent hyperventilation. In infancy, hypotonia is typical leading to feeding problems and a delay in reaching developmental motor milestones. In older children, an abnormal breathing pattern often develops, such as a period of hyperpnea followed by apnea. Epilepsy is less common but in children who do have seizures, their ECG is abnormal. Many children have a happy disposition, flapping their hands when excited and laughing without a clear reason. Their gait looks stiff, due to a combination of hypotonia and ataxia. Most adults with Pitt-Hopkins syndrome have moderate to severe cognitive impairment and will not be able to speak.

Pitt-Hopkins syndrome is a genetically heterogeneous condition caused by an autosomal dominant mutation in *TCF4.* Many different mutations have been found in the *TCF4* gene of affected children and adults, including heterozygous stop, splice, and missense mutations (1, 2).

Diagnosis

The diagnosis of Pitt-Hopkins syndrome is based on clinical features and the exclusion of other conditions with similar symptoms, such as Angelman syndrome, Rett syndrome, and Mowat-Wilson syndrome.

Molecular genetic testing of *TCF4* can be used to confirm the diagnosis.

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Management

Treatment: Manifestations of Pitt-Hopkins syndrome are treated by a multidisciplinary team specializing in the care of children with cognitive and motor impairment, including physical therapists, speech therapists, and specialists who treat epilepsy.

Genetic Counseling

Almost all mutations in the *TCF4* gene occur de novo (3). Prenatal testing may be offered to unaffected parents who have had a child with Pitt-Hopkins syndrome.

References

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