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My46 Trait Profile

Tuberous Sclerosis Complex

Tuberous Sclerosis Complex is a genetic condition that affects many organs and can cause tumors in the skin, kidney, brain, heart, eyes, lungs and other organs. It is caused by mutations in the TSC1 and TSC2 genes which makes the hamartin and tuberin proteins.

Characteristics of Tuberous Sclerosis Complex

Tuberous Sclerosis Complex (TSC) affects approximately 50,000 people in the United States and one million worldwide, with an estimated incidence of 1 in 6,000 live births.

The following systems are most commonly affected:

Brain and Neurological function:

In 95% of individuals with TSC, the brain is somehow affected. This usually takes the form of specific lesions (e.g., cortical tubers, subependymal nodules and subependymal giant cell astrocytomas) that can be detected by brain imaging.

Epilepsy is by far the most common medical condition in TSC, occurring in 80-90% of individuals. In about one third of individuals with TSC, epilepsy starts out as infantile spasms. Peak onset occurs at about 4-6 months of age.

Individuals with TSC have an increased risk of having neurodevelopmental and behavioral impairment. Although approximately 50% of individuals with TSC have normal intelligence, developmental delay and learning disabilities are commonly found in children with TSC. Additionally, up to 50% of individuals with TSC can develop autism.

Skin:

Skin lesions, including those found on the face, body and nails, are found in almost all individuals with TSC. The earliest sign may be white skin patches (hypomelanotic macules), which are best seen under ultraviolet light. As a child grows older, a characteristic facial rash across the nose and cheeks may appear.

Heart:

Cardiac (heart) involvement is common in TSC and is found in up to 66% of individuals. Benign heart tumors (cardiac rhabdomyomas) are often an early sign of TSC. Fortunately, these tumors often regress spontaneously, shrinking or completely disappearing with time.

Kidney:

Kidney lesions occur in over half of all children at the time of initial evaluation. Benign kidney lesions, which account for 75% of abnormalities, are made up of vascular tissue, smooth muscle, and fat. They usually grow very slowly and may not be problematic until young adulthood. Larger kidney lesions can cause symptoms and may require intervention.

Diagnosis/Testing

Clinical diagnosis of TSC is based on a careful physician exam in combination with imaging of the brain, heart and kidneys. Skin exams often involve the use of an ultraviolet light called a Woods lamp which may be useful for finding skin features that can be hard to see on infants or individuals with pale skin.

TSC is caused by a change or mutation in one of two genes: TSC1 and TSC2. The TSC1 gene makes the hamartin protein, and the TSC2 gene makes the tuberin protein. These proteins keep cells from growing in an uncontrolled way. Mutations in either of these genes are thought to interfere with this process. Genetic testing for TSC at this time is able to detect mutations in the TSC1 or TSC2 genes in approximately 85% of individuals. For the other 15% of individuals

without an identifiable mutation, researchers are studying ways to accurately find mutations in these two known genes and look for additional genes that may be involved.

Management/Surveillance

Individuals with TSC should have comprehensive care by a variety of specialists, ideally coordinated by a multi-disciplinary TSC clinic if possible. Ongoing management of TSC includes imaging of the brain and kidneys every 1-3 years, depending on neurological or kidney involvement, at least until the age of 21 years old. Depending on symptoms, individuals may be followed by specialists in cardiology, dermatology, epilepsy, neurology, ophthalmology and pulmonary. Neurodevelopmental testing is recommended at diagnosis and as needed at times of school entry and/or transitions to optimize educational performance. Chest computed tomography (CT) is indicated for females in adolescence/young adulthood due to the risk of lymphangio-leiomyomatosis (LAM: where normal lung is destroyed and replaced by multiple cysts).

Anti-seizure medications to prevent or control seizures are available. Laser surgery or topical medications can often correct skin abnormalities. Surgery to remove tumors can help to preserve the function of affected organs. For other symptoms of TSC, such as developmental delay, services such as early intervention, special education and other therapies are often effective in moderating symptoms.

Mode of inheritance

TSC is inherited in an autosomal dominant pattern. This means inheriting one mutation is enough for an individual to be affected and show signs of TSC. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child. In general, one third (33%) of individuals with TSC inherit the genetic condition from a parent. Two thirds (66%) of all cases are sporadic or occur for the first time in a family.

Risk to family members

The risk to family members depends on whether or not the individual with TSC has a parent affected with TSC. If a parent also has TSC, the risk of having a child with TSC is 50% with each pregnancy. If a parent does not have TSC, the risk of other siblings being affected is very low.

Special considerations

Advancements in research show great promise in developing new and improved treatment options. There are currently clinical trials ongoing for symptoms of tuberous sclerosis, see http://www.clinicaltrials.gov/ct2/results?term=tuberous+sclerosis.

Resources

Tuberous Sclerosis Alliance
http://www.tsalliance.org/
Tuberous Sclerosis Association
http://www.tuberous-sclerosis.org
Genetics Home Reference: Tuberous sclerosis complex
http://ghr.nlm.nih.gov/condition/tuberous-sclerosis-complex
Medical Home Portal: Tuberous sclerosis complex
http://www.medicalhomeportal.org/diagnoses-and-conditions/tuberous-sclerosis-complex/description

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