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My46 Trait Profile

PTEN Hamartoma Tumor syndrome

Other Names: Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome, Autism Spectrum Disorder with Macrocephaly, Lhermitte-Duclos disease, Proteus-like syndrome

PTEN Hamartoma Tumor syndrome is a group of conditions in which individuals have a higher chance to develop certain cancerous and noncancerous tumors. It is caused by mutations in the PTEN gene which makes the PTEN protein.

Characteristics of PTEN Hamartoma Tumor syndrome

PTEN Hamartoma Tumor syndrome (PHTS) refers to a number of conditions that can be caused by mutations in the PTEN gene, including Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome, adult Lhermitte-Duclos disease, autism-spectrum disorders associated with large head size (macrocephaly), and perhaps some individuals with features of Proteus syndrome.

Cowden syndrome (CS) is a rare (1 in 250,000 people) condition that causes increased risks for several cancers as well as non-cancerous overgrowth of a number of tissues. The cancer risks seen in CS includes 25-50% for breast cancer and approximately 5-10% for thyroid cancer and uterine cancer. More recently an increased risk for colon cancer, kidney cancer and melanoma has been suggested. The non-cancerous tissue overgrowths seen in CS include specific skin and mouth lesions (e.g., papules, trichilemmomas, lipomas, and acral keratoses), thyroid nodules and goiter, colon polyps, macrocephaly, and vascular anomalies.

Bannayan-Riley-Ruvalcaba syndrome (BRRS) is characterized by macrocephaly, intestinal polyps, lipomas (i.e., fatty tumors) and pigmented spots on the penis. Developmental delay and large birth weight are also seen in BRRS. Although BRRS was originally thought to be a different disease than CS, about 60% of patients with BRRS have PTEN mutations.

Lhermitte-Duclos disease (LDD) is a brain lesion defined as a dysplastic gangliocytoma of the cerebellum. The majority of adults with LDD, with or without other signs of CS/BRRS, may have PTEN mutations. PTEN mutations are less commonly found in children with LDD, however.

PTEN mutations are also seen in some children with autism spectrum disorder and macrocephaly. While some of these children have additional signs of CS/BRRS, others do not.

Diagnosis/Testing

Although it was initially thought that 80% of individuals who meet CS clinical diagnostic criteria have a PTEN mutation, more recent evidence suggests that the rate is closer to 35%. PTEN mutations are found in approximately 50-60% of those with BRRS. Standard diagnostic criteria have not been developed for the other conditions associated with PTEN mutations.

Testing criteria for Cowden syndrome have been developed for use by medical providers by the National Comprehensive Cancer Network (NCCN) as part of their Clinical Practice Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian and are updated annually (http://www.nccn.org) Although genetic changes in several other genes (e.g., KILLIN, SDH) have been suggested to be associated with PHTS, more research is needed to confirm these findings.

Management/Surveillance

Management guidelines have been developed and are updated annually by the NCCN as part of the Clinical Practice Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian. Current management recommendations for women include clinical breast exams every 6-12 months (from age 25), annual mammography and breast MRI (from age 30-35), vigilance for signs of endometrial (uterine) cancer, and consideration of preventative mastectomy (surgical removal of the breasts) and hysterectomy (surgical removal of the uterus). Recommendations for both men and women include an annual physical exam including thyroid palpation (from age 18), a baseline thyroid ultrasound at age 18 with consideration of annual repeat, colonoscopy every 5-10 years in asymptomatic people (from age 35), and consideration of annual dermatologic exams.

Mode of inheritance

PHTS is inherited in an autosomal dominant manner. This means that inheriting one PTEN mutation is enough for an individual to be affected and show signs of PHTS. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child.

Risk to family members

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

Special considerations

Although there are many syndromes that are included in PTHS, it is important to know that any individual with a PTEN mutation undergo increased cancer surveillance to detect any tumors at an early treatable stage.

Resources

Cowden Syndrome: A Guide for Patients and their Families
http://www.uihealthcare.org/2column.aspx?id=22923&terms=*cowden*
Genetics Home Reference: Cowden syndrome
http://ghr.nlm.nih.gov/condition/cowden-syndrome
The University of Texas M.D. Anderson Cancer Center: Cowden syndrome (Spanish translation of Cowden Syndrome)
http://www2.mdanderson.org/app/pe/index.cfm?pageName=opendoc&docid=2209
Bannayan-Ruvalcaba-Riley syndrome (BRRS): A Guide for Patients and their Families
http://www.uihealthcare.org/2column.aspx?id=22904

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