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My46 Trait Profile

Nevoid basal cell carcinoma syndrome

Other Names: Gorlin syndrome, Gorlin-Goltz syndrome, Basal cell nevus syndrome, fifth phacomatosis

Nevoid basal cell carcinoma syndrome is a rare genetic condition in which individuals have a higher chance to have certain cancerous and noncancerous tumors. It is mainly caused by mutations in the PTCH1 gene which makes a protein called patched-1.

Characteristics of Nevoid basal cell carcinoma syndrome

Individuals with nevoid basal cell carcinoma syndrome (NBCCS) have an increased chance of developing cancerous (malignant) and noncancerous (benign) tumors, as well as other abnormalities. Individuals with NBCCS have an inherited tendency to develop multiple skin cancers called basal cell carcinomas, which are the most common type of skin cancer. The chance of developing basal cell carcinoma is approximately 90% for individuals with NBCCS. Approximately 5-10% of children with NBCCS develop a specific type of brain cancer called medulloblastoma. Individuals with NBCCS are also at increased risk to develop cysts (i.e., benign fluid filled tumors) in their jaws called odontogenic keratocysts. Other benign tumors (e.g., fibromas) sometimes develop in the heart and/or ovaries of individuals with NBCCS. Affected individuals also tend to have bone abnormalities and most often involve the shape of the ribs (bifid or split), spine (scoliosis), and skull (large, called macrocephaly). Other features commonly seen in this condition include birth defects (like cleft lip/palate or eye abnormalities), thickening of the skin (hyperkeratosis), pits in the skin of the palms of the hands or soles of the feet, and bright spots that show up on brain imaging tests but do not typically cause problems (intracranial ectopic calcifications). The features seen in this condition are highly variable within families as well as between other unrelated, affected individuals. While intelligence is usually normal in individuals with NBCCS, up to 5% of individuals do have some intellectual disability.

Diagnosis/Testing

NBCCS can be diagnosed either by meeting certain clinical criteria or by genetic testing for a change or mutation in a gene called PTCH1. The PTCH1 gene is a tumor suppressor gene which means that it keeps cells from growing too fast. Mutations in the PTCH1 gene do not allow the patched-1 protein to work normally and as a result, cells may grow uncontrollably. This uncontrolled growth is what can cause the tumors and cysts in affected individuals.

Another tumor suppressor gene that has been identified to also cause NBCCS is the PTCH2 gene. Some individuals with medulloblastoma but without the typical features of NBCCS have mutations in a gene called SUFU.

Management/Surveillance

Management of NBCCS often includes the involvement of multiple healthcare providers including doctors specializing in the skin (dermatologist), brain (neurologist), and teeth (dentist). Many individuals with NBCCS are evaluated by a clinical geneticist to evaluate for characteristic facial features, bone abnormalities, and problems with the skin. Follow up is often annually to ensure that multidisciplinary care recommendations are being followed.

In addition to a typical dental examination, due to the increased risk for developing jaw cysts, jaw x-rays are often recommended. Additional exams often include brain imaging (to evaluate for intracranial ectopic calcifications and medulloblastoma, chest x-rays (to detect bifid ribs), ultrasounds of the heart (to detect fibromas), eye exams, spine x-

rays (to look for scoliosis), and pelvic ultrasounds in adult women (to detect fibromas in the ovaries).

It is typically recommended that individuals with NBCCS avoid radiation and excessive sun exposure to reduce the chance of developing basal cell skin cancers. Most individuals with NBCCS need surgical operations to remove tumors or cysts that develop. There are also several other ways to treat basal cell skin cancers including putting medication on the skin or having laser treatments.

Mode of inheritance

NBCCS is inherited in an autosomal dominant pattern. This means inheriting one PTCH1 mutation is enough for an individual to be affected and show signs of NBCCS. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child. Most of the time (approximately 70-80%), the condition is inherited from an affected parent.

Risk to family members

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

Special considerations

None

Resources

Basal Cell Carcinoma Nevus Syndrome Life Support Network
http://www.gorlinsyndrome.org/
Genetics Home Reference: Gorlin syndrome
http://ghr.nlm.nih.gov/condition/gorlin-syndrome
Cancer.Net: Nevoid Basal Cell Carcinoma Syndrome
http://www.cancer.net/cancer-types/nevoid-basal-cell-carcinoma-syndrome

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