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My46 Trait Profile

Hereditary Diffuse Gastric Cancer

Hereditary diffuse gastric cancer is a cancer syndrome where individuals have an inherited tendency to develop a specific form of stomach cancer. It is caused by mutations in the CDH1 gene which makes the E-cadherin protein.

Characteristics of Hereditary Diffuse Gastric Cancer

Individuals with hereditary diffuse gastric cancer (HDGC) are at increased risk of developing a specific form of stomach cancer called diffuse gastric cancer, which is also known as signet ring carcinoma or isolated cell-type carcinoma. Stomach cancer may develop at any age with the average age of onset of 38 years, however it may develop as early as adolescence. The chance of developing gastric cancer for individuals with HDGC can be as high as 80% over their lifetime. Women with HDGC are also at increased risk of developing breast cancer. The chance of developing a specific form of breast cancer called lobular breast cancer for women with HDGC is approximately 39-52% over their lifetime. Not all individuals with HDGC develop cancer.

Diagnosis/Testing

Approximately 30-50% of individuals with HDGC have a change or mutation in the CDH1 gene. This suggests that there are other genes yet to be identified that also cause HDGC. The CDH1 gene is a tumor suppressor gene which means that it keeps cells from growing too fast. Mutations in the CDH1 gene do not allow the E-cadherin protein to work normally and as a result, cells may grow uncontrollably. This uncontrolled growth is what can cause the tumors in affected individuals.

Management/Surveillance

Management of HDGC includes intensive surveillance, however early detection of diffuse gastric cancer is very difficult. Preventive surgeries such as removal of the stomach (i.e., prophylactic total gastrectomy) may be recommended for individuals with HDGC. Prophylactic total gastrectomy is very beneficial in reducing cancer risk, but risks and other considerations must be carefully discussed with appropriate health care providers before a decision is made. The gastric surgeon must be experienced with HDGC cancer risks and best technique to minimize surgical complications. Increased breast surveillance and mammography as well as referral to a high risk breast clinic is recommended for affected women due to their increased risk for developing lobular breast cancer.

It is very important that individuals with HDGC be followed closely by their healthcare providers. Referral to a high-risk cancer center with experience in managing individuals with HDGC is recommended for individuals with HDGC and for those who are at risk of having HDGC.

Mode of inheritance

HDGC is inherited in an autosomal dominant pattern. This means inheriting one CDH1 mutation is enough for an individual to be at increased risk of developing HDGC-related cancers.

Risk to family members

Every child of an affected individual has a 50% chance of inheriting the CDH1 mutation. Majority of affected individuals inherit a mutation from an affected parent. Thus, siblings of an affected individual typically have a 50%

chance of inheriting the CDH1 mutation.

Special considerations

None

Resources

No Stomach for Cancer, Inc.
http://www.nostomachforcancer.org/
Stanford Medicine Cancer Institute
http://cancer.stanford.edu/patient_care/services/geneticCounseling/HDGC.html
Genetics Home Reference: CDH1
http://ghr.nlm.nih.gov/gene/CDH1

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