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My46 Trait Profile

Familial Medullary Thyroid Cancer

Familial Medullary Thyroid Cancer belongs to a group of genetic conditions called Multiple Endocrine Neoplasia type 2 in which individuals have a higher chance to develop certain cancerous tumors. It is caused by mutations in the RET gene which makes the proto-oncogene Ret protein.

Characteristics of Familial Medullary Thyroid Cancer

Multiple Endocrine Neoplasia type 2 (MEN2) is a group of inherited conditions that increase the chance of developing tumors (overgrowth of cells) in certain endocrine (hormone-producing) tissues.

There are three main subtypes of MEN2: Familial Medullary Thyroid Cancer (FMTC), MEN2A (see MEN2 trait profile), MEN2B (see MEN2 trait profile). A certain form of thyroid cancer called medullary thyroid cancer is the most common feature of MEN2. Almost all people with MEN2 will develop this cancer at some point during their lives. The characteristics of FMTC include multiple family members with medullary thyroid cancer, and the absence of other MEN2-related tumors (e.g., pheochromocytomas tumors of the adrenal gland; parathyroid adenomas tumors of the parathyroid glands).

Diagnosis/Testing

Approximately 95% individuals with FMTC have a change or mutation in a gene called RET. The RET gene is a proto-oncogene that gives instructions to make a protein that is involved in signaling within cells. When growth factors attach to the RET protein, cells divide, mature, and take on other functions. Individuals with MEN2 have a change or mutation that over-activate the RET proto-oncogene, making it a cancer-promoting gene. Mutations in different parts of this gene are associated with specific characteristics, such as the subtype of MEN2 and the age of thyroid cancer onset.

Management/Surveillance

All individuals with FMTC will develop medullary thyroid cancer. The most effective treatment for medullary thyroid cancer is surgical removal of the thyroid (i.e., thyroidectomy) and surrounding lymph nodes. Prophylactic thyroidectomy (surgical removal of the thyroid before cancer occurs) is the main prevention for individuals who have a known RET mutation. Mutations in different parts of this gene are associated with specific characteristics, such as the subtype of MEN2 and the age of thyroid cancer onset. Typically, removal of the thyroid is recommended before age five. An individual who has their thyroid removed needs life-long thyroid hormone replacement therapy. At least once a year, blood work also needs to be performed to screen for cancer (even after the thyroid is removed).

Mode of inheritance

All MEN2 subtypes, including FMTC, are inherited in an autosomal dominant pattern. This means that inheriting one RET mutation is enough for an individual to be affected and show signs of MEN2. Most mutations causing FMTC are inherited from a parent with FMTC (95% of the time) or it can occur brand new (de novo) in an individual (5% of the time).

Risk to family members

The risk to family members depends on whether or not the individual with FMTC has a parent affected with FMTC.

If a parent also has FMTC, the risk of having a child with FMTC is 50% with each pregnancy. If a parent does not have FMTC, the risk of other siblings being affected is very low.

Special considerations

Mutations in the RET gene may also cause Hirschsprung disease (see trait profile), a condition in which a part of the large intestine does not work because it has not developed proper nerve stimulation. Hirschsprung disease can occur in some families with MEN2A or as a separate isolated condition. If Hirschsprung disease is present, surgery to remove the affected part of the large intestine is often needed.

Resources

Association for Multiple Endocrine Neoplasia Disorders
http://www.amend.org.uk
Genetics Home Reference: Multiple endocrine neoplasia
http://ghr.nlm.nih.gov/condition/multiple-endocrine-neoplasia

References

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