

Parathyroid Cancer

Subjects: Genetics & Heredity

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Parathyroid cancer is a rare cancer that usually affects people in their forties or fifties and occurs in one of the four parathyroid glands. The parathyroid glands are located in the neck and secrete parathyroid hormone, which enhances the release of calcium into the blood.

Keywords: genetic conditions

1. Introduction

In about 90 percent of cases, the early signs of parathyroid cancer are high levels of parathyroid hormone (hyperparathyroidism) and calcium (hypercalcemia) in the blood. In these cases, the cancer is described as hormonally functional because the parathyroid glands are producing excess hormone.

Many individuals with hormonally functional parathyroid cancer develop hypercalcemic crisis, in which calcium levels in the blood are very high. Neurological problems can develop, including changes in mood and depression. About 30 percent of individuals with hypercalcemia due to parathyroid cancer develop kidney and skeletal problems. These problems include increased urine production (polyuria), deposits of calcium in the kidneys (nephrocalcinosis) leading to the formation of kidney stones (nephrolithiasis), bone pain, bone loss, and increased bone fractures. Abdominal pain, inflammation of the pancreas (pancreatitis), sores (ulcers) in the lining of the digestive tract, nausea, vomiting, weight loss, and fatigue are also common.

About 10 percent of cases of parathyroid cancer are described as hormonally nonfunctional. In these cases, levels of parathyroid hormone and calcium are normal. The signs and symptoms of hormonally nonfunctional parathyroid cancer are related to the tumor obstructing nearby structures in the neck. These problems include difficulty swallowing (dysphagia) and speaking (dysarthria), a hoarse voice, shortness of breath (dyspnea), or vocal cord paralysis.

Up to 85 percent of individuals with parathyroid survive at least 5 years after they are diagnosed. The disease recurs in approximately half of individuals. If cancer does recur, it will commonly be within 3 years of the original diagnosis and up to 78 percent of people with recurrent cancer survive at least 5 years. Hormonally nonfunctional parathyroid cancer has a lower survival rate because it is often found at a later stage, as it does not have early signs such as increased calcium and parathyroid hormone levels.

In hormonally functional parathyroid cancer, death is usually caused by organ failure (usually kidney failure) due to prolonged hypercalcemia and not directly due to the tumor. In hormonally nonfunctional parathyroid cancer, the cause of death is typically related to the tumor itself, such as its impact on the function of nearby structures or its spread to other tissues (metastasis).

2. Frequency

Parathyroid cancer is one of the rarest types of cancer. It accounts for 0.005 percent of all cancers, with about 1,000 cases reported in the medical literature.

3. Causes

Cancers occur when genetic mutations build up in critical genes, specifically those that control cell growth and division (proliferation) or the repair of damaged DNA. These changes allow cells to grow and divide uncontrollably to form a tumor. In most cases of parathyroid cancer, these genetic changes are acquired during a person's lifetime and are present only in certain cells in the parathyroid glands. These changes, which are called somatic mutations, are not inherited. Somatic mutations in many different genes have been found in parathyroid cancer cells. Less commonly, genetic changes present

in all of the body's cells increase the risk of developing parathyroid cancer. These genetic changes, which are classified as germline mutations, are usually inherited from a parent. In people with germline mutations, changes in other genes, together with non-genetic factors, also influence whether a person will develop parathyroid cancer.

Mutations in the *CDC73* gene are found in up to 70 percent of cases of parathyroid cancer. In approximately one-third of affected individuals with changes in this gene, the mutation is inherited from a parent and is present in all of the body's cells. In people who have parathyroid cancer with *CDC73* gene mutations, the cancer is seven times more likely to metastasize than is parathyroid cancer in affected individuals without *CDC73* gene mutations. Individuals with *CDC73* gene mutations are also at a higher risk of recurrence of the cancer and have a decreased survival rate compared to those without *CDC73* gene mutations. Mutations in other genes have also been found in parathyroid cancer, but each of these mutations has been reported in only a small number of individuals.

The *CDC73* gene provides instructions for making a protein called parafibromin. This protein is found within the nucleus of cells throughout the body and is likely involved in gene transcription, which is the first step in protein production. Parafibromin functions as a tumor suppressor, which means it keeps cells from growing and dividing too rapidly or in an uncontrolled way. In individuals with a *CDC73* gene mutation, either inherited from a parent or acquired during their lifetime, a second mutation in the other copy of the *CDC73* gene must occur in parathyroid cells for cancer to develop. Parathyroid cells with two altered copies of the *CDC73* gene produce no functional parafibromin. As a result, cells grow and divide unchecked, which can lead to parathyroid cancer.

A significantly increased risk of parathyroid cancer is also a feature of certain rare genetic syndromes. Parathyroid cancer occurs in 15 percent of individuals with hyperparathyroidism-jaw tumor syndrome and in 1 percent of individuals with familial isolated hyperparathyroidism. These conditions are both caused by mutations in the *CDC73* gene. In rare cases, parathyroid cancer has also been found in people who have a tumor disorder called multiple endocrine neoplasia, which is caused by mutations in other genes.

Non-genetic factors have also been found to contribute to a person's risk of developing parathyroid cancer, including a history of hyperparathyroidism with chronic kidney failure, thyroid cancer, and previous radiation therapy on the neck.

The Gene Associated with Parathyroid Cancer

- *CDC73*

4. Inheritance

Most cases of parathyroid cancer are not caused by inherited genetic factors. These cancers are associated with somatic mutations that are acquired during a person's lifetime, and they do not cluster in families.

A predisposition to parathyroid cancer caused by a germline mutation is usually inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to increase a person's chance of developing a tumor. It is important to note that people inherit an increased likelihood of developing cancer, not the disease itself. Not all people who inherit a cancer-predisposing gene mutation will ultimately develop cancer.

5. Other Names for This Condition

- cancer of the parathyroid
- cancer of the parathyroid gland
- carcinoma of parathyroid gland
- malignant neoplasm of parathyroid
- malignant neoplasm of parathyroid gland
- malignant parathyroid gland neoplasm
- malignant parathyroid gland tumor
- malignant parathyroid neoplasm
- malignant parathyroid tumor
- malignant tumor of parathyroid
- malignant tumor of parathyroid gland
- parathyroid adenocarcinoma
- parathyroid carcinoma
- parathyroid gland cancer
- parathyroid gland carcinoma

- parathyroid neoplasms

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