All About Pheochromocytoma

What are pheochromocytomas?

Pheochromocytomas are very rare tumors of chromaffin cells, which are cells of the adrenal gland that make hormones called catecholamines. In pheochromocytoma, the cells produce too many catecholamines, specifically norepinephrine, epinephrine (also known as adrenaline), and dopamine, all of which are necessary for our bodies to function. Pheochromocytomas are found in the adrenal glands. Humans have two adrenals; each sit on top of a kidney. Generally, only one adrenal gland is affected by a pheochromocytoma, but there may be more than one tumor in that gland.

Tumors that are found outside the adrenal glands are known as extra-adrenal pheochromocytomas or paragangliomas. Most tumors that start in the chromaffin cells do not spread to other parts of the body and are benign (not cancerous). Despite being benign, these tumors can cause problems because of their production of catecholamines and do require treatment. A small percent of pheochromocytomas are malignant (cancerous). These are tumors that have spread outside the adrenal gland.

What causes pheochromocytoma and am I at risk?

Pheochromocytoma is rare. There are about 2 to 8 persons per million diagnosed each year in the United States. It can affect a person of any age and affects men and women equally. The only known risk factor is a genetic syndrome, which causes about 25% of cases. The four genetic syndromes associated with pheochromocytoma are: von Hippel-Lindau Syndrome (vHL), Multiple Endocrine Neoplasia Syndrome type 2A and 2B (MEN2A and 2B), Neurofibromatosis type 1 (NF1), and Familial Paraganglioma Syndrome. Speak to your provider about genetic testing and counseling if you or another family member wants to be tested for these syndromes.

How can I prevent pheochromocytoma?

There are no specific measures you can take to prevent pheochromocytoma since the only known risk factor is hereditary and you cannot alter your genetics.

What screening tests are there for pheochromocytoma?

Pheochromocytoma is a very rare type of cancer and there are no specific screening tests.

What are the signs of pheochromocytomas?

Due to the presence of extra catecholamines that are produced by pheochromocytomas, patients may have hypertension (high blood pressure), which can cause headaches, as well as sweating, pounding of the heart, chest pain, and anxiety. These symptoms can occur in "episodes," with periods of time where there are no symptoms, or they can be persistent. The frequency depends on how the tumor is causing catecholamines to be released.

The classic triad of symptoms is headaches, heart palpitations, and sweating. However, most people with pheochromocytoma do not have all three of these symptoms, and only half have at least one of these symptoms. The most common finding is hypertension, which lasts for short periods of time and may actually be normal in between elevated episodes. Keep in mind that the vast majority of patients with hypertension do not have pheochromocytoma. Some patients will present in "pheo crisis," when adrenaline is released in a dangerous amount and can cause stroke, heart attack, organ failure, coma, and in some cases death.

How is pheochromocytoma diagnosed?
In some cases, the tumor is discovered incidentally, meaning it was found during a CT or MRI of the abdomen that was performed for an unrelated reason. In patients who do have symptoms, there are blood and urine tests (such as a 24-hour urine collection) to measure the level of catecholamines in the body. Types of catecholamines tested for include vanillylmandelic acid, metanephrines, and plasma metanephrines. These are all substances that are formed as catecholamines are broken down by the body and are therefore elevated in cases of pheochromocytoma.

As far as imaging tests are concerned, CT and MRI scans are most often used to detect the tumor. A special nuclear medicine scan called a meta-iodo-benzylguanidine (MIBG) scan may be used in cases where the laboratory tests or symptoms point to a pheochromocytoma, but none is found on CT or MRI. This test uses a radioactive form of iodine, which is attached to the MIBG molecule; MIBG is structurally similar to noradrenaline. This compound is given through a vein. The patient returns to the nuclear medicine department the following day for the actual scan. This delay allows the MIBG compound to concentrate in any tumor cells. The radioactive part of the compound allows these areas of tumor to be visualized on the scan. In addition, PET scanning is being studied in the diagnosis of these tumors. Genetic testing may be suggested by your healthcare provider if you are at risk for having an inherited syndrome.

**How is pheochromocytoma staged?**

After you have been diagnosed with pheochromocytoma, tests will be done to determine if the tumor has spread to other parts of the body. Unlike other cancers, there is no standard staging system for pheochromocytomas. After diagnostic testing is complete, your team may refer to the cancer as localized (confined to one area; these are typically benign tumors), regional (spread to surrounding areas) or metastatic (spread to areas away from the original tumor).

**How is pheochromocytoma treated?**

**Surgical Treatment**

Once a pheochromocytoma is diagnosed, the treatment of choice is **surgical resection**, whether or not the tumor is benign or malignant. The resection may completely remove the tumor and adrenal gland or the tumor and only part of the adrenal gland. If the cancer has spread to other parts of the body, those affected organs and tissues may also be removed. Surgical removal usually resolves any symptoms the patient was experiencing, including hypertension. Medication is needed to manage hypertension prior to surgery to prevent any complications from high blood pressure during the surgery. Because of the possibility of fluctuating catecholamine levels during the surgery, it is a risky procedure if not done with an experienced surgeon and anesthesiologist. A few weeks following surgery, "plasma free metanephrines" (a laboratory test) are measured and if the results are normal, the resection is deemed complete.

Surgical resection can be curative in cases of localized pheochromocytoma. These tumors may metastasize (spread) to the lung, brain, and bone. If it occurs, metastatic disease tends to progress slowly over a period of many years, though there can be ongoing complications related to the elevated catecholamine levels. If both adrenal glands are removed a patient will need hormone replacement therapy.

**Radiation Therapy**

**Radiation therapy** uses high energy x-rays to kill cancer cells. These x-rays are similar to those used for diagnostic x-rays, but they are of a much higher energy. The high energy of x-rays in radiation therapy results in damage to the DNA of cells. Cancer cells divide faster than healthy cells, so their DNA is more likely to be damaged than that of normal cells. Additionally, it is harder for cancer cells to repair damaged DNA compared to normal cells, so cancer cells are killed more easily by radiation. Radiation therapy aims to kill cancer cells, while killing fewer cells in normal, healthy tissue. External beam radiotherapy is generally reserved for patients who have malignant (metastatic) pheochromocytoma which has spread to the bone. The goal of radiotherapy in such situations is to relieve symptoms, such as pain. The dose and duration of treatment will vary according to the treatment site and other patient factors, but a two-week course is common.

Metaiodobenzylguanidine (MIBG), sometimes used as a diagnostic tool for pheochromocytoma, may be used as treatment for patients with malignant disease. Diagnostic MIBG scans usually use iodine-123, which decays (becomes inactive) faster than iodine-131. Iodine-131 is used as a treatment. In other words, when given in a low dose, MIBG concentrates in areas of tumor, causing it to "light up" on a diagnostic scan. In higher doses, using iodine-131 MIBG, the radioactive iodine kills the cells that take up the MIBG. The treatment process involves an IV infusion of MIBG. Because radiation is emitted during and after the
treatment, patients must stay within a designated area for a few days, until radiation levels in the body have dropped to the point where it is safe to leave. The treatment is well tolerated, but it can suppress the production of blood cells by the bone marrow. Blood counts will need to be checked. Follow-up after treatment may include repeating a diagnostic MIBG scan; ideally, if the treatment was successful there will be decreased MIBG uptake on the scan. While MIBG treatment can be very effective, there are some malignant pheochromocytomas, which do not take up MIBG, and in these tumors, Iodine-131-MIBG therapy will not work. A test will be done prior to treatment to check if this type of therapy will work.

Chemotherapy and Targeted Therapy

Chemotherapy refers to medications that are usually given intravenously (IV, into a vein) or in pill form. Chemotherapy travels throughout the bloodstream and throughout the body to kill cancer cells. This is one of the big advantages of chemotherapy. In the case of pheochromocytoma, chemotherapy is not used as a primary treatment, but as an option for treatment of symptomatic malignant pheochromocytoma that has not responded to MIBG therapy. The most commonly used chemotherapy regimen is cyclophosphamide, vincristine, and dacarbazine. Similar to pre-surgical medical management with medication, patients being treated with chemotherapy need to have their hypertension managed beforehand. Chemotherapy can cause catecholamine release during treatment, causing high blood pressure.

Targeted therapies work by stopping or slowing the growth of a tumor by interfering with a specific molecule needed for cancer growth. Finally, newer treatments, including molecular-targeted therapies, such as sunitinib, are being studied in patients with malignant pheochromocytoma.

Clinical Trials

There are clinical research trials for most types of cancer, and every stage of the disease. Clinical trials are designed to determine the value of specific treatments. Trials are often designed to treat a certain stage of cancer, either as the first form of treatment offered, or as an option for treatment after other treatments have failed to work. They can be used to evaluate medications or treatments to prevent cancer, detect it earlier, or help manage side effects. Clinical trials are extremely important in furthering our knowledge of this disease. It is through clinical trials that we know what we do today, and many exciting new therapies are currently being tested. Talk to your provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the OncoLink Clinical Trials Matching Service.

Follow-Up Care and Survivorship

The guidelines for follow up after treatment of pheochromocytoma depends upon how you were treated and your providers will create a follow-up plan for you. If you were treated with surgery, you will most likely have to see your provider to have testing done about 2 weeks after surgery. Most patients will see their providers about every 3-4 months for 2-3 years and then less frequently the longer you do not have recurrence of disease. You will be monitored for symptoms that you had experienced prior such as high blood pressure and headaches. The levels of hormones in your blood will be monitored. It is important to communicate with your provider if you are experiencing any recurrent or new side effects or symptoms so that your provider can determine the best testing, imaging, and plan of care.

Fear of recurrence, the financial impact of cancer treatment, employment issues and coping strategies are common emotional and practical issues experienced by pheochromocytoma survivors. Your healthcare team can identify resources for support and management of these practical and emotional challenges faced during and after cancer.

Cancer survivorship is a relatively new focus of oncology care. With nearly 17 million cancer survivors in the US alone, there is a need to help patients transition from active treatment to survivorship. What happens next, how do you get back to normal, what should you know and do to live healthy going forward? A survivorship care plan can be a first step in educating yourself about navigating life after cancer and helping you communicate knowledgeably with your healthcare providers. Create a survivorship care plan today on OncoLink.

Resources for More Information

Pheochromocytoma Support Foundation

The Pheochromocytoma Support Foundation’s mission is to raise public awareness, provide information, and support those
with pheochromocytoma and their families.

www.pheosupportfoundation.org

Cancer Hope Network

Provides one-on-one support to people undergoing treatment for cancer and to their families through training individuals who have recovered from cancer and matching them with cancer patients currently undergoing a similar experience

www.cancerhopenetwork.org

Cancer Support Community

An international non-profit dedicated to providing support, education and hope to people affected by cancer.

www.cancersupportcommunity.org

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