What Is Sporadic Pheochromocytoma & Paraganglioma?

Pheochromocytoma (pheo) and paraganglioma (para) are rare slow-growing neuroendocrine tumors arising from adrenal medulla and sympathetic or parasympathetic paraganglia respectively.

There is one adrenal gland above each kidney. Pheos develop in the center of the adrenal gland in the adrenal medulla. Paras develop outside the adrenal gland, most commonly in the head, neck, chest, abdomen, or pelvis.

The term 'sporadic' refers to a pheo or para that is not linked to an inherited genetic mutation. The sporadic form of the illness has a lower chance of recurrence when compared to an inheritable form of illness.

Pheo and para can occur at any age, but most commonly affect people between the ages of 20 and 50. Recent research has indicated that as many as 1 in 3,000 will be diagnosed with pheo and para in their lifetime, but many people have symptoms for years before receiving a diagnosis.

Symptoms +/- associated syndromes

Both pheos or paras can produce an excess amount of hormones called catecholamines, which may include norepinephrine (noradrenaline), epinephrine (adrenaline), and dopamine. The release of catecholamines can cause persistent or episodic:

- High blood pressure
- Headache
- Sweating
- Flushing
- Paleness of the face
- Weight loss
- Palpitations/tremors
- Severe anxiety and other symptoms

As some of these symptoms can also be caused by multiple other conditions, the diagnosis may be delayed. Rarely, pheo and para do not cause any symptoms but may be discovered incidentally on a scan for an unrelated condition. Head and neck para usually do not produce any catecholamines. In this case, if local symptoms do not appear they may be found incidentally (during a scan for an unrelated reason).
If left untreated, a pheo or para can result in severe or life-threatening conditions, including stroke and heart attack. Early diagnosis is important, because if left untreated, pheo and para can metastasize, and ultimately, lead to death.

Causes and/or risk factors for pheo and para
We do not know exactly what causes pheo and para, but 40% of patients diagnosed have a genetic mutation. Everyone diagnosed should talk to their doctor about genetic testing. In addition, it is important to follow advice in leading a healthy lifestyle: eat healthy, exercise and avoid smoking and too much alcohol.

Common tests that may be used to help diagnose

Blood/Urine Tests

Blood and urine tests (24-hours urine collection) for measurement of metabolites of catecholamines are used for the diagnosis. These metabolites include normetanephrine (metabolite of norepinephrine), metanephrine (metabolite of epinephrine) and 3-methoxytyramine (metabolite of dopamine). The last metabolite is very useful for the diagnosis of head and neck para and may help in the diagnosis of metastases. All three metabolites are measured simultaneously in one blood sample although not all labs measure 3-methoxytyramine. Further, it is not readily available in the U.S. and may not be widely available.

Screening for potential genetic conditions is recommended as this helps guide medical care for the pheo and para patient and for their family. Genetic testing can be performed with a blood or saliva test.

Negative genetic testing does not entirely rule out an inherited cause for pheo and para. Genetics is a rapidly growing field and it is recommended that individuals check back with their medical team every few years to update their medical and family history, as it is possible that new gene associations with pheo and para will be discovered in the future.

Scans and other tests

Imaging will help to identify where, how many, and size of the tumor(s). CT and/or MRI are often used first, before functional imaging is used.

Functional imaging may include FDG PET/CT, 123I-MIBG or 68Ga-DOTATATE/DOTATOC. The choice depends on tumor location and other factors.

Pathology

It is not recommended for patients suspected of having a pheo or para to have a biopsy because manipulation of the tumor can cause a release of catecholamines resulting in a hypertensive crisis.

Treatment

There is global consensus agreement that all neuroendocrine cancer patients should be reviewed by a specialist neuroendocrine cancer multidisciplinary team to ensure best care.

If detected early, pheo and para can be successfully treated and managed in the vast majority of cases. The treatment of choice for the condition is surgery to remove the tumor(s), but in case that surgery is not possible there are other treatment options.

Before surgery

Anesthesia and manipulation of the tumor during surgery can cause a massive release of catecholamines which can result in a hypertensive crisis. To avoid this, patients must be adequately “blocked” with medication before surgery.

Alpha and beta-blockers are prescribed to normalize blood pressure and heart rate, which protect the patient from the effects of high levels of catecholamines released during surgery. First, an alpha blocking medication is prescribed for at least 2 weeks before the surgery.

Phenoxybenzamine and doxazosin are the most commonly used alpha-blocking drugs. After some days on an alpha-blocker, in most patients a beta-blocker is additionally prescribed, sometimes in combination with calcium channel blockers. Adequate oral hydration and a high salt diet may be recommended, as well.

Non-surgical treatment:

Surgery may not be possible because of advanced or metastatic disease. In this case, one or more of the approaches below may be suggested:

- Active observation. An experienced doctor may suggest only regular monitoring of the tumor(s) if they are not secreting catecholamines, there are no symptoms and the tumor(s) are stable (not growing).
- Targeted therapies, systemic chemotherapy
- External beam radiation, interventional radiology
- Targeted radiopharmaceutical (radionuclide) therapy such as ^{131}I-MIBG (only available in the U.S.) or ^{177}Lu-DOTATATE (PRRT)
- Your pheo and para specialist team may suggest consideration to participate in an appropriate clinical research study

Follow up

Long-term regular follow-up is recommended for all patients. Yearly urine or blood tests for pheo and para should be performed to detect remaining disease, return of the disease, or the development of metastases. Those with secretory pheo and para due to remaining disease or metastatic disease should let their care team know about any planned procedure so that a blocking regimen can be prescribed if needed, and they should wear a medic alert bracelet / necklace to aid in the event of an emergency. For those with a large primary tumor and/or with a genetic mutation, follow-up CT, MRI or functional imaging is recommended. Long term regular follow-up keeps those with pheo and para updated on new information, treatments and research in the field, as it becomes available.

Resources

Association for Multiple Endocrine Neoplasia Disorders
www.amend.org.uk

Pheo Para Alliance
www.pheopara.org

For the full list of INCA members: https://incalliance.org/members/