Cowden Syndrome

What is Cowden syndrome?

Cowden syndrome (CS) is a genetic condition, meaning that it can be passed to an individual from their parents. A person with CS has an increased risk to develop a variety of benign and cancerous tumors. Individuals with CS are at increased risk to develop thyroid cancer and women with CS are also at increased risk to develop breast cancer and uterine cancer. Many different benign (non-cancerous) tumors are also common in individuals with CS.

Cowden syndrome is sometimes called PTEN Hamartomatous Tumor Syndrome or PHTS. There is also a rare type of CS that is called Bannayan-Ruvalcaba-Riley Syndrome.

What are the signs and symptoms of Cowden syndrome?

Many signs and symptoms **can** be associated with CS. However, CS affects each person differently and most people with CS have some of these symptoms, but not all. Symptoms include:

- Learning disabilities, autism, and/or mental retardation
- Large head size
- Certain types of lesions or papules (bumps) on the skin (a dermatologist can recognize these) The most common are:
  - Trichilemmomas on the face
  - Papillomatous lesions, particularly if they are on the face and/or mucous membranes (such as gums). This can include a "cobblestone" appearance of the tongue or gums.
  - Keratoses (hard growths on the skin) found on the palms of the hands or soles of the feet
- High risk of developing tumors, both benign and cancerous (for more information see the next section "What are the cancer risks with Cowden syndrome?")

What are the cancer risks with Cowden syndrome?

CS is a rare condition. Because it is rare, researchers are still learning about the specific cancer risks caused by CS. If you have CS, it is important that you stay in contact with your genetics clinic so that you can stay informed about any new developments. The estimated cancer risks with CS are:

- Men and women with CS have approximately a 10 percent (%) lifetime risk to develop thyroid cancer, compared to less than 1% in the general population. The thyroid is a gland in the base of the throat that helps to make hormones. There are different types of thyroid

cancer. Follicular thyroid cancer is the most common type associated with CS. Medullary thyroid cancer is never associated with CS.

- Women with CS have a 25-50% lifetime risk to develop breast cancer. This is higher than the average women's lifetime risk of breast cancer, which is about 12%. Women with CS are also more likely to develop breast cancer at a younger age (30-49 years of age) than average.
- Women with CS may also have an increased chance of developing endometrial (uterine) cancer.
- Rarely, a type of brain tumor called Lhermitte-Duclos disease occurs in adults with CS.
- People with CS may be at increased risk for other types of cancers, such as kidney cancer.

What are the benign tumor risks with Cowden syndrome?

Individuals with CS may have an increased chance to develop the following benign tumors, which are also common in the general population:

- A goiter (enlarged thyroid) or a benign tumor in the thyroid
- Polyps in the stomach, small intestine or colon
- Uterine fibroids (benign growths in the uterus)
- Fibrocystic breast changes (a feeling of lumps and or tenderness in the breasts)
- Lipomas (benign fatty tumors) and fibromas (benign tumors of connective tissue)

What causes Cowden syndrome?

Genetic conditions are caused by changes in a person's genes. These gene changes are called mutations. Genes are the body's instruction manuals that tell the body how to grow and develop. Every person has thousands of genes. If a person is born with a mutation in one of their genes, then this gene may not work correctly and can cause medical problems.

The gene that causes CS is called PTEN. Every person has two copies of PTEN. When both copies of PTEN work correctly, they help the body prevent tumors from forming. However, when a person is born with a mutation in one of their PTEN genes, they are at high risk to develop tumors. These tumors may be cancerous or benign. A mutation in PTEN can also cause the other signs and symptoms of CS.

What are the chances of inheriting Cowden syndrome?

The parents of a person with CS may or may not have CS. It is possible for a person to be born with CS and to be the first person in their family with the PTEN mutation (this happens more than 50% of the time). However, a person with CS has a 50% (1 out of 2) chance of passing CS onto each of their children. Although Cowden syndrome cannot skip generations, each person is affected differently by CS. In addition, both men and women are equally likely to inherit CS.

Why is it important to diagnose Cowden syndrome?

An individual with CS is at increased risk to develop cancer. Even if a person with CS already has cancer, there is a risk that they may develop a second cancer. A more aggressive cancer

screening schedule can help to prevent cancer or to detect it at an early stage.

Because CS is a genetic condition, other family members of the person with CS are also at risk. Therefore, family members may also benefit from screening. Sometimes, genetic testing can identify the PTEN mutation that caused CS. In this case, genetic testing can identify family members who will need screening and those who will not.

How is Cowden syndrome diagnosed?

Usually, the first steps in figuring out if someone has CS are:

- A physical examination – including a skin check by a dermatologist who is familiar with CS.
- Family history – a genetic counselor will ask the patient for a detailed family history. This family history will help find signs of CS in the family.

If the evaluations show signs of CS, then PTEN genetic testing is usually the next step. The test, which requires a blood sample, examines the PTEN gene and may detect a mutation. If a PTEN mutation is found, then the person has CS. But the genetic test is not perfect, so if a PTEN mutation is not found, the person could still have CS. A doctor who is familiar with genetics or a genetic counselor can best interpret these tests.

If a PTEN mutation is found, then family members of a person with CS can have predictive testing. Predictive testing helps determine which family members are at risk to develop the tumors associated with CS and which ones have the same risk as the general population. Healthy family members who have a PTEN mutation can take advantage of cancer screenings and other cancer prevention measures.

How is Cowden syndrome managed?

There is no cure for CS. Because cancer is the major health risk associated with CS, it is important to follow cancer prevention and early detection screening guidelines. Cancer screening examinations are medical tests performed when a person has no symptoms. These tests help detect cancer at the earliest, most treatable stage. Screening for people with CS usually includes:

Breast Cancer Screening (Women)

- Monthly self breast examinations
- Clinical breast examinations, every six months, beginning at age 25 years
- Yearly mammogram and yearly breast MRI beginning at age 30-35 years
- Some women with CS may wish to consider having preventive surgery (removing the breasts before cancer develops).

Thyroid Cancer Screening (Men and Women)

Baseline thyroid ultrasound beginning at age 18; yearly thyroid ultrasound may be considered thereafter

Other Screening

- Yearly comprehensive physical exam starting at age 18

- Consider yearly skin exam by a dermatologist
- Women with CS should consult a gynecologist or gynecologic oncologist about their uterine cancer risk and options for screening.

Where can I find more information?

Genetic Alliance
202-966-5557
http://www.geneticalliance.org
This organization provides support to individuals and families with genetic conditions. A helpline is available to answer questions.

American Cancer Society
800-ACS-2345 (800-227-2345)
www.cancer.org
The American Cancer Society (ACS) is a voluntary national health organization with local offices around the country. The ACS supports research, provides information about cancer, and offers many programs and services to patients and their families.

Cancer Information Service
800 4-CANCER (800-422-6237)
www.cancer.gov
The Cancer Information Service (CIS) is a program of the National Cancer Institute. People who call the CIS speak with highly trained information specialists who can answer questions about cancer screening tests, risks, symptoms, how cancer is diagnosed and the latest treatments.

Susan G. Komen Breast Cancer Foundation
800-462-9273
www.breastcancerinfo.com
The Komen Foundation answers questions from recently diagnosed breast cancer patients and provides emotional support. Information is available in Spanish.

National Society of Genetic Counselors, Inc. (NSGC)
610-872-7608
FYI@nsgc.org
www.nsgc.org
This professional organization helps consumers find local genetic counseling services.