Carney Complex [1]

What is Carney complex?

Carney complex is a hereditary condition associated with: spotty skin pigmentation; myxomas, which are benign (noncancerous) connective tissue tumors; and benign or cancerous tumors, meaning it can spread to other parts of the body, of the endocrine (hormone producing) glands [2] . Symptoms of Carney complex typically develop when a person is in his or her early 20s. Skin pigmentation and heart myxomas or other heart problems are usually the first signs of the condition. The spotty skin pigmentation is found on lips, inner and outer corners of the eyes, the conjunctiva (membrane lining) of the eye, and around the genital area. Other common features of Carney complex are Cushing?s syndrome and multiple thyroid nodules (tumors). Cushing?s syndrome features a combination of weight gain, high blood pressure, diabetes, and easy bruising, caused by the overproduction of the hormone cortisol. Although people with Carney complex have an increased risk of cancer, most tumors are benign.

Carney complex is also referred to as:

- NAME syndrome ? Nevi, meaning birthmarks or moles, Atrial myxoma, Myxoid neurofibromas, and Ephelides (freckles)
- LAMB syndrome ? Lentigines, Atrial Myxoma, and Blue nevi

What causes Carney complex?

Carney complex is a genetic condition. This means that the risk of developing cancer and other features of Carney complex can be passed from generation to generation in a family through gene(s) mutations (alterations). In particular, researchers have learned more about how the gene called *PRKAR1A* is associated with Carney complex, through its involvement with regulating the body?s cell signaling with protein kinase A (PKA). Researchers believe that more than 60% of people with Carney complex have a mutation in the *PRKAR1A* gene and up to 6% may have deletions in this gene. To date, a total of 125 different *PRKAR1A* mutations have been found. Most of the mutations are unique, meaning they are identified in single families only. So far, no strong association between a particular mutation type and certain symptoms of Carney complex, such as cancer, has been seen.

People without a mutation in *PRKAR1A* typically start to show mild symptoms later in life. These people less frequently have other family members affected by Carney complex. The gene

mutation in that person is considered sporadic, meaning it occurs by chance.

Recently, mutations in the *PRKACB* gene were found in a single patient with Carney complex and also in young children with Cushing syndrome that had no other symptoms of Carney complex. Mutations in the *PDE11A* and *PDE8B* genes have also been found in younger people with Cushing syndrome but their link to Carney complex remains in question. The search for other genes that might be associated with Carney complex continues.

How is Carney complex inherited?

Normally, every cell has two copies of each gene: one inherited from the mother and one inherited from the father. Carney complex follows an autosomal dominant inheritance pattern, in which a mutation happens in only one copy of the gene. This means that a parent with a gene mutation may pass along a copy of their normal gene or a copy of the gene with the mutation. Therefore, a child who has a parent with a mutation has a 50% chance of inheriting that mutation. A brother, sister, or parent of a person who has a mutation also has a 50% chance of having the same mutation.

Options exist for couples interested in having a child when they know that one of them carries a gene mutation that increases the risk for this hereditary cancer syndrome. Preimplantation genetic diagnosis (PGD) is a medical procedure done in conjunction with in-vitro fertilization (IVF). It allows people who carry a specific known genetic mutation to have children who do not carry the mutation. A woman?s eggs are removed and fertilized in a laboratory. When the embryos reach a certain size, one cell is removed and is tested for the hereditary condition in question. The parents can then choose to transfer embryos which do not have the mutation. PGD has been in use for over a decade, and more recently has been used for several hereditary cancer predisposition syndromes. However, this is a complex procedure with financial, physical, and emotional factors for couples to consider before starting. For more information, talk with an assisted reproduction specialist at a fertility clinic.

How common is Carney complex?

Carney complex is very rare. About 500 cases have been reported worldwide. It is estimated that between 60% and 75% of cases of Carney complex run in families. The remaining 25% to 40% of cases appear to be sporadic and may be due to a de novo, meaning a new, gene mutation.

How is Carney complex diagnosed?

Carney complex is diagnosed when a person has at least two of the 12 major features listed below. People who have a close family member, meaning a parent, sibling, or child, already diagnosed with Carney complex are considered to be affected if they have at least one of the features listed.

Major diagnostic features for Carney Complex

- Spotty skin pigmentation with specific pattern and locations
- Myxoma (noncancerous tumors)
- Heart myxoma

- Breast myxomatosis
- Breast ductal adenomas
- Primary pigmented nodular adrenocortical disease (PPNAD) or abnormal result of urine test called Liddle?s test, related to Cushing?s syndrome
- Acromegaly, an increased size of hands, feet, and face due to a pituitary tumor
- Testicular neoplasm called large cell calcifying Sertoli cell tumor (LCCST)
- Thyroid cancer [3]
- Psammomatous melanotic schwannoma, meaning tumors that grow on nerves
- Blue nevi, which are blue-black moles
- Osteochondromyxoma (bone tumors)

Genetic testing for mutations in the *PRKAR1A* gene is available for people suspected to have Carney complex; if a patient has a *PRKAR1A* mutation and one of the above tumors or other conditions, then he or she is diagnosed with Carney complex. Genetic testing for the newer genes, *PRKACA, PRKACB, PDE11A*, and *PDE8B*, is not yet commercially available.

In addition, other physical symptoms have been seen in people with Carney complex. These physical signs may suggest Carney complex, but they are not considered major diagnostic features. Research is ongoing to learn more about these symptoms and their link, if any, to the condition.

- Significant freckling without darkly pigmented spots or typical pattern
- Blue nevus, if multiple and confirmed by biopsy
- Café-au-lait spots, which are light brown spots on skin, or other ??birthmarks??
- Abnormal blood test results of high insulin-like growth factor 1 (IGF-I) levels, abnormal glucose tolerance test (GTT), and/or paradoxical growth hormone (GH) response to thyrotropin-releasing hormone (TRH) testing when there is no clinical acromegaly. Also, high levels of a hormone called prolactin in the blood. This is called hyperprolactinemia and is usually paired with acromegaly.
- Cardiomyopathy, meaning diseases of the heart muscle
- Pilonidal sinus, which is an abscess in the buttock cleft
- Extended family history of Cushing?s syndrome, acromegaly, or sudden death
- Multiple skin tags or other skin lesions called lipomas
- Polyps, meaning benign growths in the colon, usually along with acromegaly
- A single, noncancerous thyroid nodule in a younger person, as well as multiple thyroid nodules in an older patient
- Family history of cancer, in particular of the thyroid, colon, pancreas, and ovary

What are the estimated cancer risks associated with Carney complex?

The risk of cancer is increased in people who have Carney complex, but the specific risk for cancer is unknown. Types of cancer reported in people with Carney complex include adrenocortical carcinoma [4], pituitary gland tumors [5], thyroid [3], colorectal [6], liver [7] and pancreatic cancers [8]. Ovarian cancer [9] in women and tumors of the testicles in men involving the Sertoli or Leydig cells has also been reported.

What are the screening options for Carney complex?

There are no specific screening guidelines for Carney complex. Suggested screening includes:

- Yearly echocardiogram [10], beginning in infancy
- Regular skin evaluations by a health care professional and self-examinations
- Yearly blood tests to check serum levels of cortisol, prolactin, and IGF-1 beginning in adolescence
- Thyroid gland examinations that may include ultrasound [11] imaging. An ultrasound uses sound waves that create a picture of internal organs.
    - General endocrine system screening
    - Testicular examinations and/or ultrasound for men

Screening guidelines may change over time as new technologies are developed and more is learned about Carney complex. It is important to talk with your doctor about appropriate screening tests.

Learn more about what to expect when having common tests, procedures, and scans [12].

Questions to ask the doctor

If you are concerned about your risk of cancer, talk with your doctor. Consider asking the following questions of your doctor:

- What is my risk of developing cancer?
- What can I do to reduce my risk of cancer?
- What are my options for cancer screening?

If you are concerned about your family history and think you or other family members may have Carney complex, consider asking the following questions:

- Does my family history increase my risk of developing cancer?
- Should I meet with a genetic counselor?
- Should I consider genetic testing?

More Information

The Genetics of Cancer [13]

Genetic Testing [14]

What to Expect When You Meet With a Genetic Counselor [15]

Collecting Your Family Cancer History [16]

Sharing Genetic Test Results with Your Family [17]

Additional Resources

National Cancer Institute
www.cancer.gov [18]

American Cancer Society
www.cancer.org [19]

Cancer*Care*
www.cancercare.org [20]

To find a genetic counselor in your area, ask your doctor or visit these websites:

National Society of Genetic Counselors
www.nsgc.org [21]

National Cancer Institute: Cancer Genetics Services Directory
http://www.cancer.gov/cancertopics/genetics/directory [22]

National Institutes of Health (NIH) Carney Complex Patient Education Handout
http://segen.nichd.nih.gov/documents/Carney_Complex_Pt_Educ_Handout_FINAL.pdf [23]

Links:
[1] http://www.cancer.net/cancer-types/carney-complex
[2] http://www.cancer.net/node/31313
[3] http://www.cancer.net/node/31262
[4] http://www.cancer.net/node/31341
[5] http://www.cancer.net/node/31384
[6] http://www.cancer.net/node/31317
[7] http://www.cancer.net/node/31274
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[20] http://www.cancercare.org/
[21] http://www.nsgc.org/
[22] http://www.cancer.gov/cancertopics/genetics/directory
[23] http://segen.nichd.nih.gov/documents/Carney_Complex_Pt_Educ_Handout_FINAL.pdf