Rhabdoid Tumor Predisposition Syndrome

Also called: RTPS or Familial Posterior Fossa Brain Tumor of Infancy

What is rhabdoid tumor predisposition syndrome?

Rhabdoid tumor predisposition syndrome increases a person's risk of developing a kind of fast-growing tumor called a rhabdoid tumor. These tumors often grow in the brain, spinal cord and kidney. They may also develop in the soft tissues, lung, skin and heart. These tumors are most common in children.

People with rhabdoid tumor predisposition syndrome are also at increased risk of developing non-cancerous tumors that grow in the nerves, called schwannomas. Schwannomas may cause painful lumps or tingling and numbness in some areas of the body. These tumors are more common in adults.

Not all people with rhabdoid tumors have rhabdoid tumor predisposition syndrome. When rhabdoid tumors develop in people without rhabdoid tumor predisposition syndrome, the tumors are called sporadic rhabdoid tumors. Only about 30% to 35% of people with rhabdoid tumors have rhabdoid tumor predisposition syndrome.

What is the tumor risk for children with rhabdoid tumor predisposition syndrome?

People with rhabdoid tumor predisposition syndrome are at higher risk of developing rhabdoid tumors than are people in the general population. This risk is highest in childhood and decreases after age 5. Older children and adults with rhabdoid tumor predisposition syndrome are at increased risk to develop schwannomas.

Although people with rhabdoid tumor predisposition syndrome are at higher risk for tumors, some people never develop them. Doctors do not yet understand why some people with rhabdoid tumor predisposition syndrome develop tumors and some do not. Further studies may help health care providers to better understand the risks.

What causes rhabdoid tumor predisposition syndrome?

The majority of rhabdoid tumor predisposition syndrome cases are caused by changes in a gene called *SMARCB1* (also called *INI1*). Genes carry information telling cells within the body how to function. The *SMARCB1* gene helps to control how cells grow, divide and die.

Most people without rhabdoid tumor predisposition syndrome carry two working copies of the *SMARCB1* gene in their cells. One copy of *SMARCB1* is inherited from the mother and one from the father. Cells from people with rhabdoid tumor predisposition syndrome carry one working copy of *SMARCB1* and one copy that is changed. This change causes the gene to not work properly. It is called a *SMARCB1* mutation.

A few children with rhabdoid tumor predisposition syndrome inherit their *SMARCB1* mutation from a parent who also has the syndrome. However, most children have a new *SMARCB1* mutation that did not

come from a parent. These children have no history of the syndrome in their family. In these cases, the gene change either happened in an egg or sperm cell when the child was formed or in one of the child's cells during pregnancy. These children are the first in their families to have rhabdoid tumor predisposition syndrome. No matter how they acquired the gene mutation, people with rhabdoid tumor predisposition syndrome have a 50% (or 1 in 2) chance of passing it on to their children.

Most people born with one *SMARCB1* mutation are healthy at birth. As they get older, the second copy of the *SMARCB1* gene might also become changed in one or more cells of the body. When this happens, those cells can develop into a tumor. This is why people with rhabdoid tumor predisposition syndrome have a greater risk of developing rhabdoid tumors and schwannomas.

Very rarely, rhabdoid tumor predisposition syndrome is caused by changes in a different gene called *SMARCA4*. Testing for this gene is guided by information from the tumor and/or family history.

How are children with rhabdoid tumor predisposition syndrome screened for tumors?

People with rhabdoid tumor predisposition syndrome should be managed by a health care provider who knows this condition well. Screening is recommended for anyone with rhabdoid tumor predisposition syndrome, even though not everyone with the syndrome will develop tumors. The goal of screening is finding and treating tumors early to allow the best outcome for patients.

Brain MRIs and abdominal ultrasounds are recommended as soon as children are diagnosed, and then regularly after that. An MRI uses magnetic fields and radio waves to make images of the inside of the body. An ultrasound uses sound waves to make images of the inside of the body.

It is possible that what is recommended may change over time as health care providers learn more about rhabdoid tumor predisposition syndrome. Because this condition is rare and complex, it is important that parents seek out and discuss all screening options for their child with a health care provider who works regularly with this syndrome.

How is genetic testing for rhabdoid tumor predisposition syndrome done?

The health care provider may suspect rhabdoid tumor predisposition syndrome after looking at a person's medical or family history. In most cases, a health care provider or genetic counselor will ask questions about the person's health and the health of other family members.

The genetic counselor or health care provider will record which family members have developed tumors, what types of tumors and at what ages these tumors occurred. From this information they will create a family tree. Health care providers and genetic counselors will look at the family tree to find out:

- If there are more cancers than normal,
- If cancers occurred at younger-than-expected ages and
- If the types of tumors match up with what might be seen in those with rhabdoid tumor predisposition syndrome.

If rhabdoid tumor predisposition syndrome is suspected in a child or other family members, the health care provider or genetic counselor will likely recommend genetic testing of the *SMARCB1* gene. In some cases, they may recommend testing the *SMARCA4* gene as well.

How is genetic testing for rhabdoid tumor predisposition syndrome done?

Testing when rhabdoid tumor tissue can be used

- Rhabdoid tumor genetic testing is best performed by starting with a sample of the rhabdoid tumor.
- DNA (genetic material) is isolated from a piece of the tumor.
- The tumor DNA is screened for any changes in the two copies of the *SMARCB1* gene using methods such as DNA sequencing. In DNA sequencing, a genetic specialist checks the lettering (spelling) of the two copies of a gene to that of a normal sample. If there are differences, the specialist then decides if those differences might have caused the tumor. Please note that other methods may also be used, especially when the results of DNA sequencing are negative or unclear. These other tests look for changes that could affect the *SMARCB1* gene but that may not be found by DNA sequencing.
- If the two *SMARCB1* mutations are found that could have led to the rhabdoid tumor forming, a separate blood sample from the person is checked to see if it shows one of these mutations.
- Finding a *SMARCB1* mutation in the blood supports a rhabdoid tumor predisposition syndrome diagnosis.
- Not finding a *SMARCB1* mutation in the blood usually means that the child has a sporadic rhabdoid tumor.

Testing when rhabdoid tumor tissue is not available

- *SMARCB1* genetic testing can be performed on a blood sample from a child with a rhabdoid tumor, even when there is no tumor for testing. In these cases, it is sometimes harder to understand the test results.
- If a disease-associated *SMARCB1* mutation is found, the patient has rhabdoid tumor predisposition syndrome.
- If no *SMARCB1* mutation is found, this does not rule out rhabdoid tumor predisposition syndrome. It is possible that a mutation is present but it was not found because of limits in the testing process. For this reason, it is best to test the blood after the rhabdoid-causing *SMARCB1* mutations have first been found in a tumor.
- If rhabdoid tumor tissue can be sampled at a future time, the tumor testing can be performed.

SMARCB1 genetic test results can provide important information for other family members. If a *SMARCB1* mutation is found, the genetic counselor will work with the family in the following ways:

- To help the family understand the cancer risks of rhabdoid tumor predisposition syndrome
- To find out if other family members should consider testing
- To help with decisions about prenatal genetic testing

Prenatal genetic testing

Parents may undergo prenatal testing to find out if the pregnancy is affected with a known *SMARCB1* mutation in the family. Testing may take place either before pregnancy occurs or during pregnancy (after the embryo is formed).

Those considering prenatal testing should work with a genetic counselor to review the pros and cons of the tests. The genetic counselor can also help parents consider how they wish to handle the results of the testing.

Testing that occurs before pregnancy—Testing that happens before pregnancy is called preimplantation genetic testing (PGT). This special type of genetic testing is done along with in vitro fertilization (IVF). PGT offers a way to test embryos for a known *SMARCB1* mutation before placing them into the uterus.

Testing that occurs during pregnancy—Testing can be used to see if a pregnancy is affected with a known *SMARCB1* mutation. A doctor gathers cells from the pregnancy in one of two ways:

- **Chorionic villus sampling (CVS)—**during the first trimester (first three months)
- **Amniocentesis—**during the second trimester or later (last 6 months)

Collected tissue can be checked for the presence of the *SMARCB1* mutation identified in the family.

Both of these tests carry minor risks and should be discussed with an experienced doctor or genetic counselor.

Special concerns

Genetic testing for rhabdoid tumor predisposition syndrome is a complex process. Those thinking about testing should take time to consider the benefits and risks. They should discuss the process with a genetic counselor before testing is done. If they choose testing, they should review the test results with the health care provider or genetic counselor to be sure they understand the meaning of the results.

Sometimes families with rhabdoid tumor predisposition syndrome can feel sad, anxious or angry. Parents who pass on a *SMARCB1* mutation to one or more of their children can feel guilty. Some people with a *SMARCB1* mutation could have trouble getting disability coverage, life insurance, or long-term care insurance in some states. More information about genetic discrimination can be found at www.ginahelp.org.

Are there other special health care needs for children with rhabdoid tumor predisposition syndrome?

People of any age with rhabdoid tumor predisposition syndrome have a higher risk of cancer. They should monitor their health and adopt healthy habits throughout life. It is important to continue to have regular physical checkups and screenings. That way, any tumor can be found early at the most treatable stage.

Other ideas for reducing the risk of cancer include the following:

- Eat a healthy diet with lots of fruits and vegetables
- Get regular exercise
- Avoid smoking or using tobacco products
- Avoid secondhand smoke
- Avoid excess sun exposure and always wear sunscreen, hat and protective clothing when out in the sun

People with rhabdoid tumor predisposition syndrome should watch closely for general signs or symptoms that could signal cancer:

- Unexplained weight loss
- Loss of appetite
- Aches, pains, lumps or swelling that cannot be explained
- Headaches or changes in vision or nerve function that do not go away

It is important to seek medical help if anything unusual appears.

What other information and resources are there for children with rhabdoid tumor predisposition syndrome and their families?

Resources about rhabdoid tumor predisposition syndrome:

- Children's Brain Tumor Research Foundation (https://cbtf.org/)
- CureSearch for Children's Cancer – Coping with Cancer (curesearch.org/Coping-With-Cancer)
- Young People with Cancer: A Parent's Guide (www.cancer.gov/publications/patient-education/young-people)
- Making Sense of Your Genes: A Guide to Genetic Counseling (www.ncbi.nlm.nih.gov/books/NBK115508/)

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