Tuberosus Sclerosis with Cortical Hamartomas (TSC)

Patient Information Series – What you should know, what you should ask.

What is tuberous sclerosis (TSC) and how can affect the fetus?

Tuberous Sclerosis is a disease with a hereditary component affecting diverse organ systems such as the brain, heart and kidney, it affects around 1: 5 000-10 000 births. Neurologic symptoms are the most severe manifestations of the disease.
Many children with TSC are afflicted by intractable epilepsy, intellectual disability, and/or autism. Deaths are typically from neurological causes, most commonly status epilepticus (uncontrolled seizures).

How does tuberous sclerosis with cortical hamartomas (TSC-H) happen?

These lesions are associated with mutations on TSC genes which produce over activation of cell division in neural network development. This results in atypical growth of the cerebral cortex and abnormal cellular differentiation of brain cells, leading to tumour production.

How are chromosomes relevant for TSC-H?

Chromosomes are where most of our genetic information is kept. We usually have 46 of them matched in pairs: 23 come from one parent and the other 23 come from the other parent. Changes in the TS genes called mutations can lead to the development of tuberous sclerosis.

There is a theory called ¨the two hit hypothesis¨ which is thought to explain the occurrence of this condition. The first “hit” occurs in the germ cells (sperm or egg) that affects either the *TSC1* or *TSC2* gene and this mutation can cause mild symptoms and some morphologic abnormalities. If a second hit occurs in the somatic cells (nervous system cells, heart cells), produce morphologic lesions such as tumours in the brain or the heart.

Should I have more tests done?

It's important to assess the baby to know more about the condition by performing:

- **Fetal echocardiography** - a specialised ultrasound of the heart of the baby during the pregnancy to rule out the presence of cardiac tumours (called rhabdomyosarcomas) .often found in association with tuberous sclerosis.
- **Fetal neurosonography** – a specialised ultrasound of the brain of the baby during the pregnancy, to rule out cortical hamartomas or other structural alterations in the brain.
- If available, an **MRI scan** can sometimes be done to provide information on the condition of the baby. This scan uses strong magnetic fields and radio waves to create detailed images of the inside of the body.
- Also, prenatal genetic counseling should be provided to outline the different diagnostic tests available for the diagnosis of the involved genetic mutations. Genetic testing includes techniques such as amniocentesis to look for problems with the number of chromosomes or structural alterations. This is done by removing small amount of amniotic fluid surrounding the fetus and sending it for analysis.

What are the things to watch for during the pregnancy?

Presently there is no fetal therapy. Nevertheless, a close follow up with ultrasound scans every 4 weeks is indicated to monitor the evolution of neurologic and cardiac tumours as well as the development of abnormal heart rhythms, (arrhythmias), fluid on the brain (hydrocephalus) or signs of heart failure (hydrops).

Delivery at a hospital with neonatal intensive care unit at 38 weeks of gestation is indicated if there are no fetal or maternal complications.

There is no contraindication for vaginal delivery. Caesarean section is preferred if fetal hydrops exist.

What does it mean for my baby after it is born?

The severity of the condition will depend on the location and size of lesions. Most TSC patients have a variety of behavioral, cognitive, and/or psychiatric problems, others may have seizures that are difficult to control.

Will it happen again?

If mom and dad have the mutations of the TSC gen (autosomal dominant) a recurrence risk of 50% is reported. If both parent carries the affected gene and alterations (mutations) in the gene arise spontaneously (De novo mutations) there is no increased risk of recurrence. This happens in about 65% of cases.

What other questions should I ask?

- What kind of prenatal testing should I perform?
- Is there any prenatal treatment for my baby?
- How often will I have ultrasound examinations done?
- Where should I deliver?
- Where will the baby receive the best care after it is born?
- Can I meet the team of doctors that will be assisting my baby when it is born in advance?

Last updated June 2023