Hypophosphatasia

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

What is Hypophosphatasia?

Hypophosphatasia is a rare abnormality that can affect the baby in the uterus. It belongs to a category of diseases that affect the bones of the developing baby and are called skeletal dysplasias. In this specific condition the bones lack their density in minerals (hypomineralized), so they become soft, thin and bowed. The bones affected are approximately all the bones of baby's body: the skull, the vertebras, the ribs and the long bones of the limbs. It seems that the clavicles (collar bones) remain unaffected.

How does Hypophosphatasia happen?

Hypophosphatasia is a rare condition and happens in about 1 in 100,000 babies. It is caused by a genetic abnormality (faulty gene). That means that there is an error in the message of the DNA in the cells. Each message of the DNA is called a gene. Each of us inherits our genes from our parents. They provide our body with instructions that influence our looks, health and behavior. In general, each person has two copies of every gene. One copy is inherited from the mother and the other from the father. Hypophosphatasia occurs due to a mistake (called mutation) in both copies of the gene known as ALPL. This gene is responsible for the synthesis of an enzyme called alkaline phosphatase (ALP) which mineralizes the bones of the baby's body. That means that both parents are carriers of a defective copy of the gene and they have no symptoms. When a pregnancy occurs there is a one in four chance that the baby will inherit both defective genes and will have the disease.

Should I have more tests done?

Hypophosphatasia can be diagnosed before birth by testing DNA taken from the baby. This can be obtained by an invasive procedure called amniocentesis after the 15th week of pregnancy (or chorionic villus sampling - CVS between the 11th and 14th week of pregnancy). By applying these methods, the cells are collected from the amniotic fluid around the baby or from the placenta to examine the DNA. These methods are used for high-risk pregnancies, such as previously affected baby. To be eligible for this testing, the mutation in the ALPL gene must be known. This means genetic testing (a blood test) must be done on the parents.

What are the things to watch for during the pregnancy?

Hypophosphatasia can also be suspected through ultrasound in pregnancy. However, other skeletal dysplasias can have similar sonographic features. Thus, the diagnosis has to be confirmed via DNA examination or/and radiographic evaluation after birth. Some women will also accumulate extra amniotic fluid around the baby. This condition is called polyhydramnios. It can stretch the uterus too much and cause early labor before the due date. It is also possible that the baby might die during the pregnancy before birth.

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

Unfortunately, babies with hypophosphatasia generally die during the pregnancy or shortly after birth, due to poor development of the lungs and respiratory failure. Other causes of death are seizures and low phosphate level in the blood. For babies who survive further, intense support will be needed by a team of specialists, such as respiratory support, physiotherapy and surgery.

Currently, no prenatal treatment exists, and pregnancy termination is an option. If pregnancy continues, follow-up and obstetric care should be as usual. Delivery should take place in a tertiary maternity center. For mild forms, replacement therapy of the affected enzyme seems like a promising treatment.

Will it happen again?

In the majority of cases the underlying cause is a recessive faulty gene, so there is a 25% risk of recurrence. This can be detected early in the next pregnancy with the same amniocentesis procedure.

.

What other questions should I ask?

- Does this look like a severe case of hypophosphatasia?
- Are there extra signs apart from the affected long bones?
- Is there a way to be sure of the diagnosis?
- How should the pregnancy be followed-up?
- Is there a treatment available during the pregnancy?
- Where and when should I deliver?
- What care will the baby receive after it is born?
- Can I meet the genetic specialist?
- Can I meet the team of doctors that will be assisting my baby when it is born in advance?

Last updated May 2022