Fetal Ambiguous Genitalia

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

What is Ambiguous Genitalia?

Ambiguous Genitalia is a rare abnormality that can affect the baby in the uterus and after birth. It refers to the unclear or uncertain appearance of the fetal external genitalia, leading to the unsuccessful determination of fetal sex. In essence, there is confusion between the presence of a clitoris or penis and between the presence of a scrotum or labia. Thus, it is impossible for the doctor who performs the fetal ultrasound to say if the baby is a boy or a girl.

How does Ambiguous Genitalia happen?

Ambiguous Genitalia is a rare condition and happens in about 1 in 5,000 babies. The most common cause of ambiguous genitalia is a condition called congenital adrenal hyperplasia. Most mild cases are expected to be isolated. However, the condition can also be part of a chromosomal abnormality or syndrome.

The external genitalia becomes differentiated at approximately 9 weeks of gestation and genital development is typically complete by 12 weeks for girls and 14 to 16 weeks for boys. Successful development of the external genitalia for boys depends on a hormone called dihydrotestosterone (DHT) and which is the most powerful male hormone (androgen); for girls, vulvar and vaginal development is not hormone-dependent.

Without DHT action (because of either a lack of DHT or a failure of DHT to function), a genetically male fetus could appear to have female external genitalia. On the other hand, androgen exposure in a female fetus can cause labial fusion or clitoromegaly and labial enlargement. Androgen exposure may occur from maternal ingestion of hormones, maternal or fetal ovarian or adrenal tumors, or deficiency of an enzyme called P450 aromatase.

The most common cause of ambiguous genitalia, congenital adrenal hyperplasia (CAH), is a sexual development' disorder of a genetically female fetus (leading to masculinisation of the female fetus) caused by an enzymatic deficiency that disrupts the production of steroids. In 90% of cases, the deficiency is in the 21-hydroxylase enzyme, which causes an excess of 17-hydroxyprogesterone hormone, which in turn increases the production of male hormones.

Male fetuses remain unaffected with the exception of possible hyperpigmentation and penile enlargement. This enzyme deficiency also reduces two other hormones, aldosterone and cortisol, which can produce life-threatening salt-wasting in the neonatal period.

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Should I have more tests done?

Ambiguous genitalia is often diagnosed postnatally during the early newborn assessment, although prenatal diagnosis arises when fetal sex cannot be determined at the second trimester anatomy scan. Rarely diagnosis can be made later during pregnancy. Whenever ambiguous genitalia is seen a detailed ultrasound examination is indicated.

The genetic sex determination is crucial and can be easily done through new techniques involving DNA testing in maternal blood. When additional ultrasound findings are present fetal DNA testing is required through an invasive procedure called amniocentesis. Applying this method we collect cells from the amniotic fluid around the baby or from the placenta and we examine the DNA inside them. Congenital adrenal hyperplasia can also be detected with genetic and hormonal tests performed to the neonate and the parents.

What are the things to watch for during pregnancy?

Usually, the course of pregnancy progresses uneventfully. In families with congenital adrenal hyperplasia, a hormone called dexamethasone should be administered to the pregnant woman from 6 weeks of gestation. This treatment can minimize the effects of excess androgens on fetal genitalia and the developing brain. If the fetus is confirmed to be a boy, steroids should be discontinued. Follow-up scans every 4 weeks are used to monitor the growth and evolution of fetal genitalia. Obstetric care follows the standard protocol but delivery should be in a tertiary center.

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

Treatment of a newborn with ambiguous genitalia should be performed by a multidisciplinary specialist team, including geneticists, pediatric endocrinologists and pediatric urologists. There is controversy concerning sex assignment and the need or not for reconstructive surgery.

Will it happen again?

In the case of congenital adrenal hyperplasia, the underlying cause is a recessive faulty gene, so there is a 25% risk of recurrence (1 out of 4 cases). This can be detected early in the next pregnancy with an invasive procedure.

What other questions should I ask?

- Does this look like a severe case of ambiguous genitalia?
- Are there extra signs apart from the affected genitalia?
- 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?

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