Antenatal Diagnosis of Ambiguous Genitalia in a Fetus at 28th Gestational Week

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To discuss an ambiguous genitalia case diagnosed antenatally. A fetus with ambiguous genitalia has been determined during US scan performed during 28th gestational week and confirmed with physical exam postnatally. External genitalia evaluation should be a part of routine anomaly screening as ambiguous genitalia can be life threatening issue especially in enzyme defects according to the deficient enzyme type

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Ambiguous genitalia reflects a situation where the external genitalia are not clearly male or female. Intersex disorders are rare and complex; yet, in each case of genital ambiguity, accurate and expeditious management is required of the clinician. Ambiguity of the genitalia is a congenital anomaly that may be the result of defects in gene expression or the influence of environmental factors on gene expression. With the introduction of ultrasonography (US) of the fetus visualization of the genitalia has become possible. Fetal sex can be assigned reasonably accurately from 12 weeks of gestation onwards. Whilst ambiguity of the genitalia can occasionally be detected at the time of routine US, it is more commonly found when at a detailed US detecting other abnormalities or when it is performed because of a relevant family history.

Thus far, several case series have been published on the prenatal diagnosis of ambiguous genitalia.[1-4] There is one study that assessed the accuracy of the prenatal diagnosis of abnormal genitalia; they reported complete accuracy in male and 46 % in female fetuses.[5]

Case Report

Twenty- eight years- old primigravida women whose gestational week was 28 according to her last menstrual period, referred to our hospital because of severe preeclampsia. After the first evaluation, we confirmed the diagnosis of severe preeclampsia and we decided to perform Doppler USG. In Doppler USG there was absent end diastolic flow in the umbilical artery. While we were evaluating the biophysics profile, we found an ambiguity in the fetal external genitalia. We applied cesarean section for fetal stress. After the operation we confirmed the diagnosis of ambiguous genitalia. We looked karyotype and it was 46 XY. In postnatal USG of the neonate, testes were visualised in the inguinal channel. In the history, mother took propylthiouracil since 16th week of gestation for hyperthyroidism. And there was not any other significant anamnestic data.

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Discussion

Human sexual differentiation is a highly complex process under the control of multiple genes and hormones.[6-8] Abnormalities in normal sexual differentiation are relatively common and occur in approximately 1 per 4500 live births.[9] Congenital adrenal hyperplasia (CAH) is the most common diagnosis in 46XX cases presenting with ambiguous genitalia. Those with 46XY have a wider range of diagnoses.

The diagnostic steps that must be taken immediately following the birth of an infant with genital abnormalities include a complete family and pregnancy history, a thorough physical examination, measurement of blood glucose, 17 OHP, serum electrolytes and renal function tests. An urgent chromosomal analysis (particularly a chromosomal count) should be performed.

With current ultrasound machines structurally abnormal genitalia can be detected as early as 15 weeks of gestation.[10] The suspicion of ambiguity of the genitalia can arise under several circumstances, including a reduction in penile size for gestational age or an absent phallus, curvature of the phallus, scrotal phallic malposition or fusion, apparent fusion of the labia or indeterminate sex. The other stimulus to the diagnosis is when discordance between the US fetal sex and the fetal karyotype is identified. It is not always possible to differentiate between clitoromegaly and micropenis unless there is nor-

mal development of the scrotum with evidence of testicular descent. As determining the fetal male gender is based on the identification of a penis and scrotum, it did not take long to focus attention on testicular descent. In 1983 Birnholz[11] reported that the testes do not descend into the scrotum before 26 weeks of gestation. In that study, 62% of fetuses had descent at 28-32 weeks and 95 % after 32 weeks. Fifteen years later these results were confirmed by Achiron et al.[12], who also developed a nomogram for scrotal circumference, showing that scrotal size increases with gestational age. To assist in assessing the development of the fetal penis, reference ranges for penile length were constructed.[13,14] The penile length increases from 3.9 mm at 14 weeks of gestation to 23.8 mm at 38 weeks. Development of the fetal uterus at 19–38 weeks has also been studied.[15] The uterus was measured on an axial view through the fetal pelvis at the fetal bladder level. Both the transverse diameter and the circumference of the uterus have been measured successfully in 78 % of the study population, and there was a linear association with gestational age.

In our case, because of the gestational age was 28 weeks, fetal gender has been identified easier. One of the other advantages of us was the diagnosis of preeclampsia. Because we wanted to evaluate this preeclamptic patient more detailed with a sophisticated USG machine which has a better resolution to perform Doppler USG. The diagnosis of genital ambiguity is more reliable in male fetuses. In one study the accuracy of the prenatal diagnosis of abnormal genitalia is reported complete accuracy in male and 46 % in female fetuses.[5] And our fetus was male as well.

External genitalia defects due to exposure of propylthiouracil are not common. Hypospadias is the only reported defect of external genitalia due to propylthiouracil exposure[16]

Fetal US can be used to accurately predict gender from around 12 week of gestation. Fetal sex assignment in the first trimester can be useful in pregnancies at risk of severe sex-linked diseases, in disorders involving ambiguous development of the genitalia, and in determining zygosity in multiple fetuses. Prenatal diagnosis of ambiguous genitalia can assist in the diagnosis of many malformation syndromes, and in other cases alert the health professional and parents to the possibility of underlying hormonal abnormalities that may require urgent intervention in the newborn period. Mostly sonographers encounter to great interest of the families about the fetal gender which sometimes can be a very boring situation for themselves. And many sonographers try to determine the fetal gender after the request of the families.

In conclusion, as ambiguous genitalia can be life threatening issue especially in enzyme defects according to the deficient enzyme type, external genitalia evaluation should be a part of routine anomaly screening.

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