

# A case of male pseudohermaphroditism with an abnormal triple analyte screening result

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## ÖZET

**Anormal triple analyte tarama sonucu verem bir erkek psödohermafrodit vakası.**

Down sendromu için gebelikte yapılan bir taramada yüksek riskli bir hasta saptandı, çünkü human karyonik gonadotropin seviyesi yüksek, ankonjuge östriol seviyesi düşüktü. Amniosentez yapıldı ve karyotip 46XY olarak bulundu. Doğumda ise bebeğe erkek psödohermafrodit tanısı konuldu. Bunun 3β-OH dehidrogenaz eksikliğine bağlı olduğu anlaşıldı. Biz hastadaki triple analyt tarama sonucunun, bu enzimin eksikliği ile ilgili olmadığını inanıyoruz.

**Anahtar Kelimeler:** Karyonik gonadotropin, ankonjuge estriol, erkek psödohermafroditizm.

## SUMMARY

During a routine screening program for Down's syndrome, a patient was detected to be in the high-risk group, because the human chorionic gonadotropin level was high and the unconjugated estriol level was low. An amniocentesis was performed and the karyotype was 46 XY. However, at delivery the infant was found to be a male pseudohermaphrodite due to 3β-OH dehydrogenase deficiency. We believe that the result of the triple analyte screening can not be related to this enzyme deficiency.

**Key words:** Human chorionic gonadotropin, unconjugated estriol, male pseudohermaphroditism.

## INTRODUCTION

During a routine screening program for Down's syndrome, a patient was detected to be in the high-risk group and an amniocentesis was performed. The karyotype was 46 XY and the antenatal follow-up of this pregnancy was uneventful. However, at delivery the infant was found to be a male pseudohermaphrodite. A suspicion has arisen about whether male pseudohermaphroditism can be the cause of the high risk results of this pregnant women or this is a coincidence.

## CASE REPORT

A 17 year old primigravid woman was followed throughout her pregnancy and except for the triple analyte screening test for Down's syndrome all her

physical examinations and laboratory tests were found to be normal. At 17 weeks of gestational age (confirmed both by her last menstrual period and ultrasonographical fetal biometry) a triple analyte screening test for Down's syndrome and for open neural tube defects was performed. The maternal serum alpha-fetoprotein (MSAFP) was 34.00 ng/ml (1.0 MoM), the human chorionic gonadotropin (hCG) was 52.00 IU/ml (2.36 MoM) and the unconjugated estriol (uE3) was 0.90 ng/ml (0.65 MoM). The risk for open neural tube defects was calculated as 1: 12000. While the age related risk for our patient of delivering an infant with Down's syndrome is 1: 1230, the risk calculated after the test was 1: 262. Although the accepted cutoff value for offering karyotyping is 1: 250 in our institution, because of the

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parent's anxiety an amniocentesis was performed at 18 gestational weeks. The karyotype was 46 XY and during the follow-up the ultrasonographic examination of the external genitalia were evaluated as male. After birth, the pediatric examination of the newborn was diagnosed as a male pseudohermaphrodite. There was incomplete labioscrotal fusion, the labioscrotal ridges were prominent and the gonads were palpable in the labioscrotal ridges. The phallus was measured as 0.8x0.5 cm. After the pediatric endocrinology follow-up of the newborn, a partial deficiency of 3  $\beta$ -OH dehydrogenase is decided to be the etiology of this disorder.

## DISCUSSION

As a definition a male pseudohermaphrodite has testes, but external and sometimes internal genitalia take on female phenotypic aspects. The causes of this developmental disorder can be antimüllerian hormone defect, impaired androgenization, androgen insensitivity syndromes, 5-alpha reductase deficiency, testosterone biosynthesis defects, P450 scc deficiency, 3  $\beta$ -OH dehydrogenase deficiency, 17 alpha-hydroxylase deficiency (P450c117), and 17  $\beta$ -OH dehydrogenase deficiency. The etiology of this disorder can be chromosomal, genetic (recessive or dominant), polygenic/multifactorial or teratogenic (1,2).

Since male pseudohermaphroditism is not a common disorder, a prenatal screening test has not been formulated. The newborn in our case has a 3  $\beta$ -OH dehydrogenase deficiency. This disorder is characterized with a decreased synthesis of both androgens and estrogens. The major androgen produced is dehydroepiandrosterone (DHA).

The triple analyte screening is an algorithm based on gestational age, race, maternal weight, ma-

ternal age and analyte values for MSAFP, hCG, and uE<sub>3</sub> and has been devised to calculate a patient's specific risk for Down's syndrome. The individual MoM values are used to calculate likelihood ratios (3). In our case especially the hCG level is high and the uE<sub>3</sub> level is low.

Steroidogenesis in the fetal-placental unit does not follow the conventional mechanisms of hormone production in a single organ. The fetal and placental compartments are complementary and form a complete unit (1). In pregnancy, approximately 90 % of maternal estriol is derived from fetal precursors. The principal mission of the fetal adrenal is to provide DHA sulfate for placental estrogen production. The high output of DHA sulfate by the fetal zone is due to low 3  $\beta$ -OH dehydrogenase gene expression. Estrogen feeds back to the adrenal to provide even more of this precursor. After birth, there is no exposure to estrogen and the fetal adrenals switch to the adult type of the gland. Because of the enzyme deficiency in our case, there is still a high output of DHA and the estrogen levels are low. The low levels of the uE<sub>3</sub> during pregnancy can not be related to this deficiency since there is already a low expression of this enzyme in the fetal adrenals.

We could not find any information about the placental function in pregnancies of pseudohermaphrodite fetuses. The high levels of hCG in fetuses with Down's syndrome is related to the immaturity of the placenta. In our case we can not make a conclusion about the high levels of hCG.

We believe that in this pregnancy the abnormal result of the triple analyte screening and the fetus with male pseudohermaphroditism is merely a coincidence.

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