

Selective Feticide of The Aneuploid Fetus in a Twin Pregnancy: A Case Report s

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An obstetric ultrasound of a 38 years old woman with a dichorionic diamniotic twin pregnancy showed an increased nuchal translucency and absent nasal bone in one of the fetuses suggesting us an increased risk for Down Syndrome (DS). This fetus was detected to have trisomy 21 (47, XX+21) by investigation of the amniocentesis material and was selectively undergone feticide process at 20 weeks of gestation. The other fetus (46, XX) was successfully delivered at 36 weeks without any complications.

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Case Report

A 38 years old woman at her fourth pregnancy admitted to our outpatient clinics for antenatal follow-up. Her husband was 37 years old. She had had three previous blighted pregnancies and this last pregnancy was achieved by an assisted reproductive technology (ICSI) after a period of infertility. The other risk factors for this pregnancy were a heterozygote mutation for methylene tetrahydro folate reductase, gestational diabetes regulated by meticulous insulin treatment, autoimmune thyroid disease and a positive antinuclear antibody titer. The patient used enoxaparine sodium 2000 IU/day subcutaneously and aspirin 80 milligrams/day throughout her pregnancy.

This was a dichorionic diamniotic twin pregnancy. An obstetric ultrasound performed at 14 weeks of gestation revealed a pathologically increased nuchal translucency and absence of the nasal bone in one of the fetuses while the other fetus seemed to be normal. We performed amniocentesis to both gestational sacs after informing the parents about the risks of the procedure and the risk of having a child with DS at this age and with these ultrasound findings. The karyotype analysis from the materials obtained by amniocentesis revealed that that the fetal karyotypes were 46, XX and 47, XX+21. Parents were given detailed information about trisomy 21 and were offered the approach of selective feticide with all of the risks of the procedure being told. They accepted the procedure, and, at 20 weeks of gestation the fetus with the abnormal karyotype was selectively terminated by

blood aspiration from the heart of fetus until cardiac arrest occurred. This was managed by a transabdominal needle under ultrasound guidance. No complications occurred. The patient was hospitalized with a diagnosis of preeclampsia at 35th gestational week. The other fetus survived during the rest of the pregnancy and at 36th gestational week a phenotypically normal female infant of 2460 grams with an apgar score of 9 which was otherwise healthy was delivered by cesarean section due to development of preeclampsia. The placentas of both twins and the abnormal fetus are shown in figure 1 and 2.



Figure 1a. During cesarean section, normal placenta with dark color and the abnormal fetus

Discussion

DS screening during pregnancy is one of the most important issues of antenatal surveillance. DS is the most frequently seen chromosomal abnormality at birth and is the most important cause of mental retardation. The risk of DS directly increases with the maternal and paternal age.¹ Patients below 35 years of age may undergo screening tests which utilize some maternal serum and some ultrasound markers.

Currently, 'triple test' is the most commonly used screening method for DS.² It uses second trimester maternal serum

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screening markers in combination with maternal age. These markers are unconjugated estriol (uE3), human chorionic gonadotropin (hCG) and alpha-fetoprotein (AFP) levels.³ Triple test results, when evaluated with maternal age and gestational age by an artificial network was shown to be useful for the detection of genetic disorders and fetal well-being.⁴



Figure 1b. During cesarean section, normal placenta with dark color and the abnormal fetus

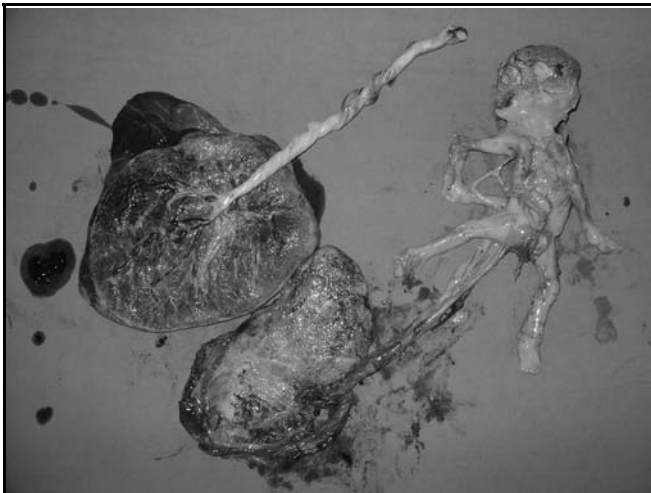


Figure 2a. Both placentas (normal and the abnormal)

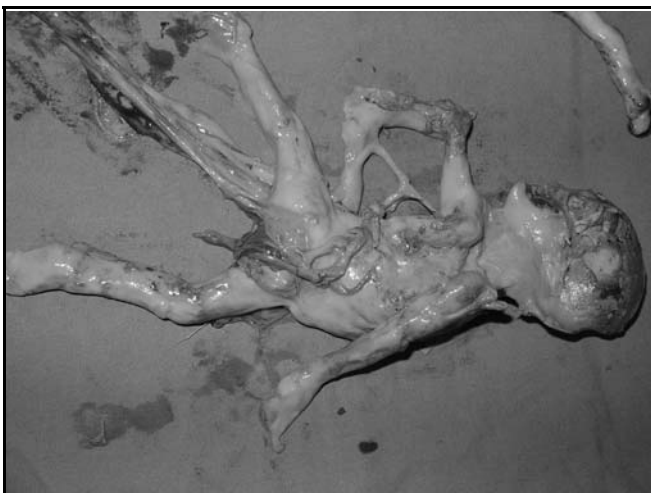


Figure 2b. Abnormal fetus (47, XX+21)

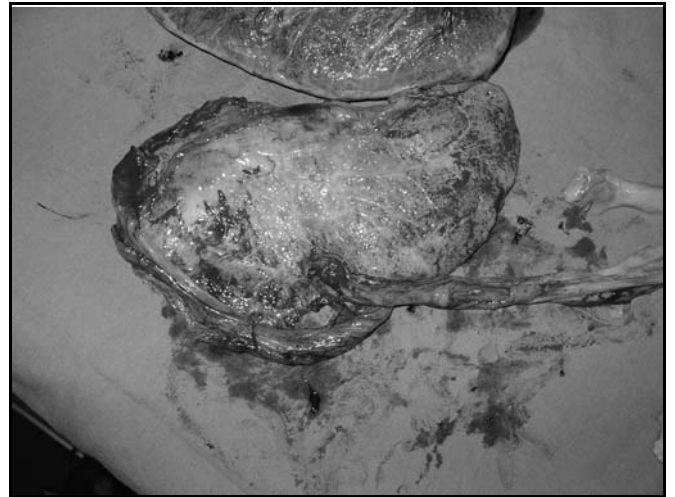


Figure 2c. Its' placenta with pale color

Ultrasound screening at 16 to 20 weeks is one of the most commonly used genetic screening tests during pregnancy. A genetic ultrasound involves a detailed evaluation for major anomalies and the identification of less specific, "soft" sonographic markers for fetal aneuploidy including thickened nuchal fold, shortened humerus or femur, intracardiac echogenic focus, echogenic bowel, renal pelvic dilation, mild ventriculomegaly and choroid plexus cysts.⁵ Soft markers are more common in the second trimester of pregnancy while prevalence of major anomalies increase with advancing gestation. These soft markers are associated with an increased risk of fetal aneuploidy, and in some cases with nonchromosomal problems. But their absences do not necessarily indicate reduced fetal risk.⁶ Identification of soft markers for fetal aneuploidy requires correlation with other risk factors, including history, maternal age, and maternal serum testing results.

The ultrasound marker nuchal translucency (NT) is known to be an effective screening tool for trisomy 21. An increase of NT was also observed in most other chromosomal abnormalities, a large number of major cardiac defects, skeletal dysplasias, and other genetic syndromes,⁷ and Werdnig Hoffman Syndrome.⁸ By using NT, about 75% of trisomical pregnancies can be identified with an invasive method rate of 5%.⁷ Two serum markers, pregnancy associated plasma protein A (PAPP-A) and free β -hCG, and NT can be used together (the 'combined test' or the 11-14th gestational week screening test) to estimate the risk of DS in the first trimester. It was shown that an integrated sonographic and biochemical test at 11 to 14 weeks can potentially identify about 90% of trisomy 21 fetuses for a false-positive rate of 0.5%.⁹ Absent nasal bone in the late first trimester has also been described recently as an important screening marker for DS.¹⁰ This ultrasound finding is also common in other aneuploidies than in normal karyotype fetuses.¹¹ The availability of these first trimester markers is mostly limited to referral centers.

In our daily practice, we mostly use the triple test and ultrasound screening for women below 35 years of age. We offer amniocentesis to women at or above 35 years of age and

for those who are screen positive for prenatal diagnosis of DS. As a result of the recent developments in maternal serum screening and second-trimester ultrasonography, many women choose to undergo noninvasive testing before deciding to undergo amniocentesis or not.¹² But these screening tests have higher false-positive rates at advanced maternal age.

Prenatal diagnosis in a twin pregnancy is a more complex issue. The screening methods that we can use are limited in these cases. In twin pregnancies we can not rely on serum markers. Because, serum marker levels in twin pregnancies are approximately twice those found in singleton pregnancies.¹³ More women with twin pregnancies are found to be false positive for DS when tests depending on serum markers are used. Use of ART causes a change in fetus-placental endocrinologic metabolism which is reflected as higher hCG levels in the ART pregnancies. First-trimester NT measurement in twin pregnancies is not affected by the problems encountered in serum screening.¹⁴ This sonographic screening approach enables a fetus-specific identification of those fetuses at high risk of DS and is associated with a lower false-positive rate than mid-trimester serum screening.

Several challenges are present in determining the most appropriate screening test modality for DS screening in ART twins. We need further studies to see whether there is any significant benefit of adding first-trimester biochemistry or nasal bone scanning in screening ART-conceived twins. Invasive tests are more difficult to perform and carry more risks for the pregnancy. Sampling of amniotic fluid from both sacs is recommended in diamniotic twin pregnancies if one (or both) of the fetuses has ultrasound abnormalities, even if the twins are apparently monochorionic.¹⁵ A young couple previously had an infant with regular DS (47, XY+21) and the next pregnancy was a twin pregnancy. Even though the mother was 27 years old and the sonographic findings were normal, amniocentesis for both twins were performed at 18 weeks of gestation for the possibility of chromosomal aberration. Unfortunately one fetus had DS (47, XX+21) while the other was normal (46, XX). In this case selective feticide was successfully performed at 20 weeks of gestation. A healthy female infant was born at 36 weeks of gestation.¹⁶ Structural anomalies are seen more commonly in twin pregnancies than in singletons. In approximately 1-2% of twin pregnancies an anomaly affecting only one fetus is diagnosed.¹⁷ In such a situation, either expectant management or selective feticide can be performed. Selective feticide can cause the death of the unaffected fetus (in about 7.5% of multiple pregnancies). The family should decide between the two after being informed about the risks and benefits of the two approaches. Type of chorionicity is very important if selective feticide will be performed. In a dichorionic pregnancy, since there are no vascular anastomoses between the two placentas, KCL (potassium chloride) injected into circulation of the affected twin will not pass to the healthy fetus. This can also be managed by intracardiac NaCl injection to

the affected fetus.¹⁸ The process of selective feticide is more complex in a monochorionic pregnancy. Both arterial and venous flows in the umbilical cord of the affected fetus should be occluded completely and permanently to prevent damage to the other fetus. In monochorionic twins bipolar cord coagulation under ultrasound guidance is associated with 70-80% survival rates.¹⁷ Intrathoracic injection of amniotic fluid to create a tamponade is reported as an alternative management for fetal reduction.¹⁹ High-intensity focused ultrasound was shown to be an alternative method for fetal reduction in an animal model.²⁰

Our case was a dichorionic twin pregnancy; selective feticide was performed by blood aspiration from fetal heart with a transabdominal needle under ultrasound guidance. The procedure was finished when cardiac arrest occurred. No complication occurred and the co-twin was delivered by cesarean section at 36th gestational week. Here, we want to mention that blood aspiration from fetal heart can be used as an alternative way of selective feticide in dichorionic twins.

Finally as far as we know, previously, intracardiac blood aspiration was not commonly performed in twin feticide. In this article we presented our case with feticide by using intracardiac blood aspiration for the first time in our country. It needs more skillful clinical experience.

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