

Crown-rump length discordance in dichorionic twins in the first trimester: different obstetric outcomes

Discordância do comprimento crânio-caudal em gémeos bicoriônicos no primeiro trimestre: diferentes desfechos obstétricos

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Abstract

First trimester intertwin crown-rump length (CRL) discordance has been suggested to predict adverse perinatal outcomes. In dichorionic diamniotic pregnancies its etiology is poorly understood. We report the cases of two sets of dichorionic twins with crown-rump length discordance diagnosed in the first trimester of pregnancy with different obstetric outcomes. In the first case, no specific cause to justify the discordant growth was found, with the pregnancy ending in a preterm birth due to severe intrauterine growth restriction of fetus 2. The second case was associated with triploidia of the smallest fetus, with normal development and birth of the co-twin.

The role of first trimester ultrasound in predicting an adverse perinatal outcome is still controversial and the optimal management of twin pregnancies with CRL discordance is a challenging question.

Keywords: Crown-rump length discordance; Dichorionic twin pregnancy; Fetal growth restriction; Fetal growth discordance

INTRODUCTION

In the last decades, there has been an increase in twin pregnancies caused by medically assisted reproductive technologies and advanced maternal age. These pregnancies represent an increased risk of perinatal morbidity and mortality, mainly due to preterm birth, growth discordance, fetal anomalies and complications related to monochorionicity^{1,2}.

Many studies demonstrate that discordance in crown-rump length (CRL) in the first trimester ultrasound can predict adverse perinatal outcomes such as fetal loss, weight discordance, fetal anomalies and preterm delivery^{1,3-6}. In dichorionic twin pregnancies, discordance can result from both intrinsic causes (such as genetic factors) and extrinsic causes (uteroplacental factors)^{3,4,7}.

Intertwin CRL discordance proportion is calculated as a percentage of the value of the larger twin ($100 \times (\text{larger CRL} - \text{smaller CRL}) / \text{larger CRL}$). However the threshold value of CRL discordance is controversial, varying between 5% and 20%⁷.

CASE DESCRIPTION

Case report 1:

A 33-year-old caucasian primigesta woman was referred to the hospital for prenatal management of dichorionic diamniotic twin pregnancy, obtained after ovulation induction therapy. Her personal and family medical history was unremarkable. First trimester ultrasound was performed at 12 weeks + 6 days and revealed fetus 1 with CRL of 65,9mm, nuchal translucency of 2,0 mm (<95th centile), nasal bone present and normal ductus venosus pulsability index (DV PI). Fetus 2 had CRL of 53,3mm (discordance of 19%), nuchal translucency of 1,5 mm (<95th centile), nasal bone present and abnormal DV PI. Combined test screening for chromosomal abnormalities was low risk

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for both fetuses (T21 1:12053 and 1:27912; T18 1:6605 and 1:66737, respectively in fetus 1 and 2 and T13 <1:100000 in both). Ultrasound reassessment at 16 weeks + 6 days showed discordant fetal growth (estimated fetal weight (EFW) of 182 grams in fetus 1 and 110 grams (<5th centile) in fetus 2), no fetal abnormalities were found. An invasive prenatal diagnostic procedure was proposed. An amniocentesis was performed at 18 weeks + 4 days, being the karyotype of both fetuses 46, XY. Detailed ultrasound scan at 20 weeks +4 days was normal in both fetuses with biometry on centile 44 in the first twin and centile 0,2 in the second. Serial ultrasound scans were performed in twins and, despite discordant growth (centile 82 and centile 0.2 at 24 weeks + 6 days, respectively), they showed normal amniotic fluid volume (AFV) and normal pulsatility index (PI) at umbilical artery (UA), middle cerebral artery (MCA) and DV. At 25 weeks +4 days, she came to the emergency department with regular painful uterine contractility, presenting a cervical length of 11mm with funnelling. She was hospitalized at our unit, for tocolysis and steroid therapy for fetal maturation. The clinical situation stabilized and she was discharged after 2 days with cervical length at 11mm. Fetal ultrasound reevaluation at 27 weeks +6 days showed fetus 1 with biometry on centile 63 (estimated fetal weight (EFW) of 1158 grams), active movements and normal AFV, UA and MCA Doppler and normal PI DV; fetus 2 with biometry on centile 0.4 (EFW 637 grams), active movements, normal AFV, UA PI at 95th centile and centralization signs with MCA PI at 5th centile, but PI DV normal. In view of the worsening clinical situation, she was transferred to a tertiary hospital with differentiated perinatal support. Regular maternal-fetal surveillance was kept until 31 weeks +4 days, when elective cesarean section was decided due to severe intrauterine fetal growth restriction in the fetus 2 with deterioration of doppler fluxometry. The first twin was born with 2005 grams and Apgar score of 9/10/10 and second twin with 800 grams (birthweight discordance of 60%) and Apgar score of 8/9/9. During hospitalization at the neonatal intensive care unit, the first twin developed respiratory distress syndrome and neonatal jaundice requiring phototherapy. The second twin developed respiratory distress syndrome with metabolic acidosis, neonatal jaundice requiring phototherapy, as well as neonatal cholestasis. The echocardiographic evaluation of the smaller twin revealed thickening of the right ventricle wall, with the remaining examination apparently nor-

mal. They presented favorable evolution, the first twin being discharged 39 days after birth with 3145 grams of weight and the second twin 70 days after birth with 2020 grams.

Case report 2

33-year-old caucasian woman, gravida 2 para 1 (previous pregnancy uneventfully with eutocic delivery of a healthy child), with an unremarkable past medical, surgical and family history, was referred to our hospital for investigation and management of a spontaneous dichorionic diamniotic twin pregnancy. First trimester ultrasound at 13 weeks + 4 days revealed fetus 1 with CRL of 46.2mm, nuchal translucency of 1.6mm (<95th centile), and fetus 2 with CRL of 74.6mm (discordance of 38%), nuchal translucency of 2.9mm (>95th centile). Both fetuses had nasal bone and normal DV PI. Combined test screening for chromosomal abnormalities was low risk for both fetuses (T21 1:1055 and 1:11226; T18 1:12687 and 1:41485; T13 1:10127 and 1:71167, for fetus 1 and 2, respectively). Ultrasound reevaluation 2 weeks later showed fetus 1 with an estimated weight of 97 grams, oligohydramnios, decreased fetal movements and normal DV PI. Fetus 2 had an EFW of 211 grams, normal AFV, normal fetal movements, normal DV PI and hyperechoic cardiac focus. Amniocentesis was performed at 16 weeks. In the post-amniocentesis ultrasound control, severe oligohydramnios and bradycardia (97 beats per minute) were seen in fetus 1. Detailed ultrasound scan and echocardiogram at 21 weeks +4 days was apparently normal in the fetus 2, being impossible to perform biometry and complete evaluation in the fetus 1, because it was "collapsed" against the uterine wall and bradycardia was maintained (110 bpm). Ultrasound re-evaluation 2 weeks later showed fetus 1 with no cardiac activity. Definitive result of fetal karyotypes was known: fetus 1 was found to be affected by triploidy 69, XXX and fetus 2 was normal 46, XX. The fetal evaluation was performed on a regular basis by ultrasonography, with growth in the 75th centile, normal AFV and normal UA and MCA Doppler. A healthy female newborn was born by eutocic delivery, at 38 weeks and 3 days, with a weight of 3960 grams and 49.7cm in length and Apgar score 9/10/10.

DISCUSSION

Traditionally, first trimester growth has been thought

to occur at a constant exponential rate with little biologic variation and intertwin growth discrepancy could emerge during the second half of pregnancy^{3,4}. It is well known that twin growth discordance in the third-trimester is associated with several adverse perinatal outcomes, such as stillbirth, preterm birth, respiratory distress syndrome, admission to neonatal intensive care unit and neonatal death. Some studies have suggested that many factors may affect growth earlier than previously thought and discordant growth may start in the first trimester. However, the role of intertwin CRL discordance in the prediction of this outcomes is controversial^{3-5,8,9}.

CRL discordance is frequently recorded in twins, but its etiology is poorly understood. It can represent a normal constitutional variant related to the different genetic potential (especially if they are of opposite genders) or to the physiologically unequal placental share of each fetus, reflecting the individual growth potential and not a pathologic condition^{3,4}. However, higher degrees of discordance in early pregnancy might predict fetal loss, birthweight discordance, intrauterine growth restriction (IUGR), chromosomal abnormalities or structural malformations^{5,7-11}. Due to this association, CRL discordance is frequently a reason to alert parents to possible adverse pregnancy outcomes, although, the cut-off above which discrepancy should be considered pathologic is controversial. Several cut-offs and different definitions of pregnancy outcomes are reported by different studies, making it difficult to compare and reach uniform conclusions. D'Antonio et al. in a systematic review concluded that intertwin discordance of $\geq 10\%$ at 11-13 weeks was associated with an increased risk of adverse pregnancy outcomes, namely perinatal loss, fetal loss >24 weeks, birth weight discordance and preterm delivery before 34 weeks.¹ This association was also found in the study by Grand et al, stating that it increases significantly in severe CRL discordance cases of $\geq 16\%$ ⁵. In contrast, other authors believe that an intertwin weight difference <15% should be considered physiological and that 25% is the threshold above which discordance should be considered as abnormal.^{6,10} It is important to keep in mind that many articles about this subject do not differentiate between monochorionic and dichorionic twins. This makes it difficult to take conclusions because discordant growth, in the first type, is almost always the result of twin-twin transfusion syndrome or selective intrauterine growth restriction from unequal sharing of the placenta. The American

College of Obstetricians and Gynecologists considers twins discrepancy as a 15-25% difference in weight among twins⁹. Two recent large European series, assessing the predictive role of CRL discordance, demonstrated a weak association between discordant birthweight and growth restriction, after considering only dichorionic twins^{7,8,11,12}. However, when comparing results of different studies, it is evident the lack of consensus on the threshold of discordance which is associated with complications (between 5% and 20%)⁷.

We report two cases of crown-rump length discordance in the first trimester in dichorionic/diamniotic twin pregnancies, surveilled in a primary hospital, with different obstetric outcomes.

In the first case, despite the early intertwin discordance (19% in the first ultrasound), the amniotic fluid, and umbilical and middle cerebral arterial Doppler remained normal until the third trimester of pregnancy. The growth discrepancy worsened throughout pregnancy, so it was necessary to end the pregnancy in a preterm birth due to severe IUGR of the smallest fetus. In the postnatal period, newborns presented a favorable evolution, being discharged without any serious complication. This case is in accordance with a large number of prior published studies that demonstrate an association between CRL discordance and intrauterine growth restriction/birthweight discordance^{2-4,6,11}.

Discordance in early fetal growth has been also associated with chromosomal abnormalities and structural malformations, particularly when the intertwin disparity is large, being the affected fetus smaller than expected^{1,3-5,8,11,13,14}.

In the second case, with a major discrepancy (38%), beside the discordant growth, the smallest fetus presented early changes in amniotic fluid. This fetus was found to be affected by triploidy with normal dizygotic co-twin. In the second trimester, fetal loss of the aneuploid twin occurred, with normal development and growth of its co-twin. Regarding the euploid fetus, despite presenting an increased nuchal translucency in the first trimester, no specific cause was found, being the morphologic evaluation and echocardiography normal, and with spontaneous resolution. Our case is in accordance with prior published studies, suggesting that the risk of fetal anomalies is increased when there is a large CRL discordance in the first trimester¹. Still, there are relatively few articles on the extent of delayed fetal growth in first-trimester discordant twins affected by severe chromosomal or structural anomalies, and therefore further studies are needed⁵. Nevertheless, this

may reflect the severe growth delay in aneuploid fetuses, as observed in aneuploid singletons pregnancies.¹³

Although CRL measurements are of limited value as a screening test to predict complications, it identifies a subset of patients at increased risk.³⁻⁵ The main advantage of the first trimester ultrasound in the early detection of intertwin growth discrepancy is the ability to stratify the obstetric risk and provide close follow up of these pregnancies. Currently, there is no clear evidence on the ultrasound surveillance frequency or even the optimal time of delivery that should be performed in dichorionic discordant twins, to eventually optimize perinatal outcomes, making it difficult to counseling facing this situation.

CONCLUSION

The role of first trimester ultrasound in predicting an adverse perinatal outcome is still controversial, with optimal management of twin pregnancies with CRL discordance being a challenging question. First-trimester CRL discordance can be related to chromosomal anomalies, especially if associated with other ultrasound abnormalities. For the remaining cases, there is also an increased risk of IUGR and growth discordance at birth, and therefore it should be considered as a high risk subgroup among multiple pregnancies. Further studies are mandatory to evaluate the strength of association between discordant CRL and adverse outcomes. They should also provide further evidence-based clinical recommendations on fetal surveillance and interventions to potentially decrease the risk of perinatal morbidity and mortality.

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