Selective intrauterine growth restriction and vascular abnormalities of monochorionic placentation

Restrição seletiva do crescimento intrauterino e patologia vascular das placentas monocoriônicas

Ana Ehrhardt Pinheiro¹, José Nona², Álvaro Cohen³, Odília Nascimento⁴, António Marques Valido⁵

ABSTRACT
It is reported the clinical case of a biamniotic monochorionic twin gestation, with selective intrauterine growth restriction diagnosed at 18 weeks in the second twin and significant weight discordance, with intermittently absent end-diastolic umbilical artery flow. Possible etiology, diagnosis, classification, clinical outcome and prognosis are discussed. This is not a situation of wide acceptance yet, but in recent studies it seems to identify a subgroup with a high risk of death in the smaller twin and neurological damage in the other one.

Keywords: Pregnancy, multiple; Fetal development; Fetofetal transfusion; Umbilical arteries/ultrasonography

INTRODUCTION
Multiple gestations account for approximately one percent of all pregnancies, but the incidence seems to be increasing in the developed world in the last few years, mainly due to fertility treatments and older maternal age(1). Perinatal morbidity and mortality in twins is three to seven times higher than in singletons(2). Dizygotic is more common than monozygotic twinning, and of those, only 30% are monochorionic (MC)(3). Chronicity determines the degree of perinatal risks and outcome, and MC twins are associated with higher rates of prematurity, low weight, neurological morbidity and mortality(2). In MC placentas, vascular sharing between placental territories of both twins invariably occurs. In about 20 to 25% of the cases, preexisting or new anastomoses are responsible for major circulatory derangements. These communications of placental vascular anastomoses may, in part, contribute to the adverse outcome of these pregnancies and are related to the major complications: selective intrauterine growth restriction (SIUGR), twin-to-twin transfusion syndrome (TTTS) and twin reversed arterial perfusion (TRAP) sequence. Fetal Doppler ultrasound allows, in some of these situations, the establishment of the diagnosis and outcome, and also to identify the pregnancies that may benefit from fetal intervention. The...
increased morbidity and mortality, with all the related complications, require careful obstetric surveillance of MC gestations in prenatal specialized health centers.

CASE REPORT

It is presented the clinical case of a biamnionic MC twin gestation with surveillance at a referral perinatal center, with SIUGR diagnosed at 18-weeks gestation in the second twin. In these situations, the obstetric evaluation protocol includes a weekly Doppler ultrasonography. Evidence of progressive growth discordance and increased umbilical artery (UA) resistance in the second twin prompted maternal hospitalization at 25 weeks of gestation. During hospital staying, amniotic fluid, bladder, weight and UA flow in the first twin were always normal. On the other hand, at 28 weeks of gestational age, intermittently absent end-diastolic flow was found in the second twin (Table 1).

Table 1. Ultrasonography and Doppler examinations comparing some parameters between both twins

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Parameters</th>
<th>1st twin</th>
<th>2nd twin</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 weeks</td>
<td>AF</td>
<td>N</td>
<td>IUGR (&lt; P_{25})</td>
</tr>
<tr>
<td>+</td>
<td>Weight</td>
<td>P_{25}</td>
<td>N</td>
</tr>
<tr>
<td>1 day</td>
<td>Arterial Doppler</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>27 weeks</td>
<td>AF</td>
<td>N</td>
<td>Increased resistance in the UA</td>
</tr>
<tr>
<td>+</td>
<td>Weight</td>
<td>P_{10}</td>
<td>Severe IUGR (P_{10})</td>
</tr>
<tr>
<td>0 days</td>
<td>Arterial Doppler</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>28 weeks</td>
<td>AF</td>
<td>N</td>
<td>Increased resistance in the UA</td>
</tr>
<tr>
<td>+</td>
<td>Weight</td>
<td>P_{5-50}</td>
<td>Severe IUGR (&lt; P_{10})</td>
</tr>
<tr>
<td>0 days</td>
<td>Arterial Doppler</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N</td>
<td>Intermittently absent end-diastolic flow in the UA</td>
</tr>
</tbody>
</table>

AF: amniotic fluid; N: normal; IUGR: intrauterine growth restriction; UA: umbilical artery; P: percentile.

A single course of antenatal corticosteroids to accelerate fetal lung maturation was given and a cesarean section, programmed. Because of signs of acute fetal distress with persistent bradycardia in the growth restricted twin, an emergency procedure was performed. Two female infants were delivered, the first one weighing 1,204 g and the second one, 589 g, with Apgar Scores of 8/9 and 2/5, respectively. Both were intubated and put on mechanical ventilation. The second twin, with SIUGR and a single UA, showed hypotension and hemoglobin levels of 5.4 g/dl and immediately upon admission to the Neonatal Intensive Care Unit (NICU), received red blood cell transfusion, inotropic drugs and hydrocortisone. Despite all therapeutic support measures, progressive worsening of the clinical state was observed, with severe anemia, thrombocytopenia, leukopenia, refractive hypotension, oligoanuric acute renal failure and persistent hypoglycemia. On the fourth day of life, metabolic acidosis, anasarca, hemoperitoneum, and pulmonary hemorrhage ensued with multiorgan failure and death. Post-mortem examination confirmed anasarca, bilateral hydrothorax, pulmonary, gastric and cerebellar hemorrhage. No placental histology was performed.

The first twin hemoglobin level was 18.8 g/dl and had a good clinical outcome, with no major intercurrences. Transfontanellar ultrasound, echocardiogram, ophthalmologic evaluation and auditory evoked potentials were normal. Follow-up at 24 months of life showed a satisfactory psychomotor development and no evident neurological abnormalities.

DISCUSSION

Multiple gestations are associated with higher rates of almost every potential complication of pregnancy, with the exceptions of post-term pregnancy and macrosomy. Short and long term perinatal morbidity and mortality are higher in twins, mainly because of gestational complications, preterm labor and uteroplacental insufficiency\(^{(2)}\), highest in MC gestations\(^{(3)}\). Intrauterine growth restriction and congenital anomalies, more frequent in twinning\(^{(4)}\), also contribute to an uncertain prognosis and to justify the need for appropriate and close prenatal assessment.

MC twinning represents a complex hemodynamic situation in which two fetal circulations are connected at the level of the placenta, by means of vascular arterio-arterial (AA), arteriovenous (AV) and venovenous (VV) anastomoses\(^{(5)}\), which may cause acute or chronic twin-to-twin transfusions\(^{(6)}\). The number, type and volume of these anastomoses, as well as the amount of acute events during pregnancy, account for the balance between the two fetal circulations and, consequently, for the occurrence of part of the major complications associated to MC gestations.

The polyhydramnios/oligohydramnios sequence, increase of amniotic fluid volume in one sac and decrease in the sac of the other twin, should raise the suspicion of TTTS\(^{(7)}\). This situation, which complicates 10 to 20% of MC gestations\(^{(8)}\), accounts for 15% of perinatal mortality in twins\(^{(3)}\), TTTS may be acute, due to sudden hemodynamic changes that usually occur during delivery, or more commonly, chronic\(^{(5)}\). Net shunting of blood from one twin (donor) to the other (recipient) results in donor fetus hypovolemia and oliguria, and recipient fetus volume overload and polyuria. This hemodynamic derangements result in a cascade of events that may culminate with perinatal demise of either twin\(^{(6)}\). The diagnosis of TTTS requires the presence of some ultrasound-based criteria: monochorionicity, single maximal vertical pocket.
of amniotic fluid 2.0 cm or lower on one side of the dividing membrane and equal or greater than 8.0 cm on the other side(6-7). After the diagnosis has been established, the severity may be classified according to the Quintero Staging System(3,6).

TRAP sequence, also called acardia, is seen in about 1% of MC twins(6). The presence of AA or VV anastomoses allows for one fetus (pump) to perfuse the other (acardiac), in a retrograde fashion. The perfused twin intakes through the UA deoxygenated blood, resulting in maldevelopment(6).

Intrauterine growth restriction occurs in approximately 10% of MC twins, and typically affects only one of the fetuses(6,8). When there is growth discordance, and the estimated fetal weight of one of the twins is below the 10th percentile, the condition is known as SIUGR(6-8). Despite significant overlapping with TTTS, SIUGR appears to be a distinct condition, but in 50% of the patients they may coexist(8). Unequal placental sharing is the most important factor determining the appearance of growth discordance, but the clinical evolution is largely influenced by the pattern of placental anastomoses(9). Preterm labor occurs most times, and spontaneous death of the growth restricted fetus may occur, increasing the risk of death (up to 26%) and neurological impairment (up to 60%) in the other twin(8). Recently, Gratacós et al. defined a classification system for SIUGR based on UA Doppler flow, correlating three types with a different clinical behavior and with different patterns of placental anastomoses(7).

Doppler study may define one of three major patterns of UA end-diastolic flow: present (Type I), persistently absent or reversed (Type II) and intermittently absent or reversed (Type III or cyclical pattern). Type I is considered, generally, to have a benign prognosis; in Type II there seems to exist a higher risk of hypoxic deterioration and neurological impairment, and Type III shows an atypical and unpredictable clinical outcome, with increased sudden fetal death of the SIUGR twin and parenchymal brain damage in the normal size twin(7,9-10). This seems to result from important AA anastomoses, which generate a cyclical pattern of UA end-diastolic flow, with acute twin-to-twin transfusion(9), and acute exsanguination episodes of the normal fetus to the smaller one. For this reason, some ongoing studies are assessing fetal intervention (in uterus) with the main purpose of placental dichorionization, using laser fetoscopy(6,9).

In the present clinical case, there is major growth discordance between both twins, and the smaller twin had an estimated fetal weight below the 10th percentile. A progressive deterioration of UA Doppler in the growth restricted twin was observed, with evidence of UA end-diastolic flow intermittently absent. This finding determined the anticipation of the delivery. The criteria for TTTS were not met: the polyhydramnios/oligohydramnios sequence was not observed, both bladders were visible and not discordant. Thus, the possible etiology is Type III SIUGR, with major AA anastomoses. Since this circulatory pattern is intermittent, it is not possible to know how long before the diagnosis was established. This fact, associated to gestational age at the time of diagnosis, frequency and blood volume of each transfusion episode during absent or reversed end-diastolic flow, are the main predictors of an unexpected outcome in the appropriate for gestational age twin. The difference between hemoglobin concentrations in both twins (5.4 g/dl versus 18.8 g/dl) is probably related to the possible existence of acute episodes of twin-to-twin blood transfusions, through the major AA anastomoses, associated with this SIUGR pattern, and seems to be the reason for the poor outcome in the growth restricted twin – hypovolemic shock and death.

This case report tried to briefly review some of the MC gestations associated complications, with emphasis on a rare clinical entity, Type III SIUGR. In recent studies, this newly described entity seems to identify a subgroup at a higher risk of death in the smaller twin and of neurological impairment in the other.

It is also emphasized the need for an early recognition and close surveillance of MC gestations, and a long term follow-up of these children.

REFERENCES