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Medicine

FIRST REPORT OF CASES OF TWIN-TWIN TRANSFUSION SYNDROME TREATED IN PORTUGAL

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ABSTRACT Twin-twin transfusion syndrome (TTTS) is the most serious complication of monochorionic/biamniotic (MC/BA) twin pregnancies1. TTTS is thought to occur in 5 to 15 % of twin MC pregnancies1,2. TTTS is a medical emergency. It is important to readily recognize it so we can avoid its complications: 80-100% mortality rate in non-treated cases and high risk of neurological sequellae in surviving fetuses1,12,13. Our medical centre started performing fetoscopic laser coagulation of the vascular anastomoses in April 2017. As far as we are concerned no portuguese medical center has yet reported in the literature the performance of such technique. To the best of our knowledge, until April 2017 all cases of TTTS in Portugal were treated in a foreign country. Hereby we describe two clinical cases of TTTS fully treated in Portugal.

KEYWORDS : Fetoscopy; Fetofetal Transfusion; Pregnancy, Twin

Introduction

Twin-twin transfusion syndrome (TTTS) is the most serious complication of monochorionic/biamniotic (MC/BA) twin pregnancies[1]. TTTS is thought to occur in 5 to 15 % of twin MC pregnancies[1,2]. *Wenstrom and Gall* pointed out monochorionic twins occur in approximately 0.7% of all pregnancies[3], which means one could assume TTTS occurs in approximately 0.07% of all pregnancies[4]. We think this can clearly be an under-estimate as assisted reproductive techniques (ART) represent nowadays a significant percentage of pregnancies in general and have been contributing to an increase in rates of twin pregnancies in particular. In Portugal, in 2016 there were born 86254 children[5], which leads us to an estimate of some 600 MC twin pregnancies, and around 60 cases of TTTS/year.

TTTS is caused by vascular anastomosis between both fetuses sharing one placenta. In fact, vascular anastomosis exist in every twin MC pregnancy, but TTTS only occurs in some of them[6,7,8]. TTTS does not usually present with maternal symptoms at its beginning. Diagnosis is made by ultrasound when we find one fetus with polyhydramnios - a deep vertical pocket of 8 cm or more in the sac of the recipient twin - which is secondary do polyuria, while the other fetus has anydramnios - 2 cm or less in the sac of the donor twin, due to anuria[9,10]. This is the classic presentation of TTTS, also called twin oligo-polyhydramnios sequence – TOPS, but there is at least one other way of presentation of vascular imbalance: TAPS syndrome: twin anemia-polycythemia syndrome, which occurs when one fetus has anemia and the other one has polycythemia, without major differences in amniotic fluid volume. TAPS syndrome is caused by imbalanced very thin vascular anastomosis[11].

TTTS is a medical emergency. It is important to readily recognize it so we can avoid its complications: 80-100% mortality rate in non-treated cases and high risk of neurological sequellae in surviving fetuses[1, 12,13]. Gold standard treatment for TTTS is fetoscopic laser coagulation of the vascular anastomoses, with the aim of completely separate fetal circulations, which is associated with survival rates of both fetuses of 35 to 69%[14,15,16] . Additionally, this procedure aims to reduce substantially neurological morbidity in surviving twins[15]. However, this treatment still has complications: in utero fetal demise, premature rupture of membranes, and chorioamnionitis.[17]. Moreover, indeed, in up to 33% of treated pregnancies inter-twin vascular connections may remain patent[18,19]. These residual patent anastomoses can cause severe complications such as TAPS and/or recurrent TTTS in up to 21% of cases [16,20]. Our medical centre started performing fetoscopic laser coagulation of the vascular anastomoses in April 2017. As far as we are concerned no portuguese medical center has yet reported in the literature the performance of such technique. Hereby we describe two clinical cases of TTTS fully treated in Portugal.

This is a case-report study of the first two TTTS-complicated MC/BA twin pregnancies treated with fetoscopic laser coagulation of the vascular anastomoses at Centro Hospitalar de Vila Nova de Gaia/Espinho. Diagnosis of monochorionicity was made during first trimester, based on absence of lambda sign. We use Quintero staging system for disease severity grading. Surgery is proposed for all cases from stage II to IV. For stage I, we propose it for severe polyhydramnios in the recipient in a symptomatic *gravida*. We use a Storz fetoscope with 1.2 or 2 mm, through a non-rigid trocart: a 10 Fr Cook Medical Check-Flo® Introducer Set. We use both linear and curved sheaths, according to localization of the placenta. We use a 400 µm laser fiber, and a maximum power of 40 watts. Before the procedure we administer a 100 mg rectal dose of indomethacin and a prophylactic dosis of cefazolin. Intervention is guided also by ultrasound. At the beginning of the procedure, we collect amniotic fluid for fetal karyotype and culture. We preferably use Solomon technique for laser ablation of anastomosis. At the end of the procedure we perform amniodrainage, in order to achieve a 5 cm maximum vertical pocket, and send some amniotic fluid for bacterial culture. After the procedure we provide analgesics according to complaints. We perform a control scan at 12 and 24 hours the procedure, and then again after 48 and 72 hours. We usually manage the patient in an outpatient setting after the third post-operatory day. We perform a control scan after one week, and after that every two weeks. A fetal magnetic resonance imaging scan is performed at 30 weeks gestation, searching for possible clastic lesions. Delivery is scheduled, if possible, to 35 weeks.

Case reports

Case report 1

This was a 39-year-old woman, IIIG0P (one first trimester miscarriage, 1 ectopic pregnancy), spontaneous MC/BA pregnancy followed in our tertiary care unit. Other medical personal and familiar history was irrelevant, except for her moderate smoking habits. Diagnosis of monochorionicity was made at 12 weeks and her first trimester combined screening for aneuploidies was considered low-risk. She was followed, as usual in MC pregnancies, with a scan every two weeks after 16 weeks, and with routine consultations and blood analysis, which were always unremarkable. At 21 weeks and 2 days, a TTTS Quintero Stage 4 was diagnosed: hydrops in the recipient, umbilical artery (UA) reversed end-diastolic flow and inverted ductus venosus (DV) a-wave. A *LASER* ablation of anastomoses was performed without complications at 21 weeks and 3 days. Twelve hours after the procedure the recipient fetus had no ascites (only had pericardial effusion) and had normal Dopplers. The donor twin had its bladder visible. By 22 weeks an echocardiographic examination was performed, revealing normal cardiac function of this twin, but signs of severe tricuspid regurgitation, and reduced pulmonary artery flow were seen in the recipient twin. She was discharged at the third post-operative day. The *gravida* only referred mild pain at trocart introduction spot that yielded with paracetamol. At the 11th post-operatory day, with 23 weeks and 1 day, both fetus had mild pericardial effusion. The ex-recipient fetus had a MCA-PSV around 0.8 MoM, biventricular hipertrophy, mild tricuspid insufficiency, and a mildly diminished pulmonary artery flow. The ex-donor had a MCA-PSV around 1,5 MoM. These changes in MCA-PSV were confirmed in a 24 hour interval and a TAPS diagnosis was confirmed. Selective feticide of the ex-recipient fetus was performed by cord ligation using a bipolar forceps. By the 4th post-operative day (24 weeks) the ex-donor fetus maintained a low MCA-PSV and showed a moderate pericardial effusion. By 24 weeks and 2 days, signs of fetal anemia included MCA findings, pericardial effusion and ascites. In this same day, intra-uterine blood transfusion was performed, in an uneventful manner. This procedure was done as an inpatient, having this patient been discharged the next day, in which MCA-PSV was normal, pericardial effusion was stable, and no signs of ascitis was seen. Cervix length was 33 mm. Four days later, with 24 weeks 6 days, this woman was again admitted in our high risk pregnancy unit due to short cervix (22 mm) associated with a mild bloody vaginal discharge and irregular uterine contractility. Ultrasound evaluation revealed a live ex-donor fetus, with MVP of AF 32 mm, normal Dopplers and no signs of fetal anemia. No clinical or analytical signs of infection were seen. She entered into labor and at 25 weeks 1 day and a c-section was done for breech presentation. The newborn weighed 480 g, and Apgar score was 4/6/7 (1st, 5thand 10th minutes). Hemoglobin was 6.6g/dL, and umbilical pH was 6,92, base excess -14 mmol/L. No clinical or analytical signs of infection were seen. Mechanical ventilation was needed since admission in neonatal intensive care unit (NICU). The need for incremental oxygen support was seen in the first days of life, despite the several surfactant doses administered. Cardiovascular stability was tried with the help of vasoactive drugs, but the newborn died at the third day of life.

Case report 2:

This was a 35 year old woman, G4P1, with a MC/BA twin pregnancy. First trimester combined screening was low risk. There was no relevant medical history. She was referred to our unit from another hospital at 22 weeks for TTTS stage 2 of Quintero. Echocardiographic evaluation revealed biventricular hypertrophy and left ventricular outflow tract obstruction in the recipient fetus. *LASER* ablation of vascular anastomosis was done by the Solomon technique, in an uneventfull manner. The patient was discharged at the third post-operative day. The last evaluation done before discharge already revealed visible bladder in the ex-donor, normal dopplers and normal amniotic fluid volume in both sacs. There were no signs of TAPS. Ex-recipient maintained biventricular hypertrophy and left ventricular outflow tract obstruction. The patient was discharged on progesterone and nifedipine.

There was resolution of the TTTS and the echocardiographic findings resolved by 27 weeks after the procedure. The patient was admitted at 28 weeks+5d at the referring Hospital due to preterm rupture of membranes. She went into labor and delivery was at 30 weeks +3d by cesarean section, due to suspition of *abruptio placentae*. The newborns are now 4 months old and are doing well.

Discussion:

For the first time in the literature there is a report of fetal surgery for TTTS in Portugal. To the best of our knowledge, until April 2017 all cases of TTTS in Portugal were treated in a foreign country. These case reports present our initial institutional experience with fetoscopic laser photocoagulation for the treatment of TTTS. The results presented here were obtained during our initial experience and represent elements of a learning curve. The fact that one Portuguese Medical Institution has capacity for treatment of these cases mitigates the need to refer these patients with these conditions abroad. We think this clearly represents an evolution of the capacity of care of our National Health System , brings social and emotional benefits to the pregnant woman and their families, and allows public budget savings.

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