

Application of Amnioreduction for Treatment of Twin-to-Twin (Feto-Fetal) Transfusion Syndrome

Yusupbaev R. B., Gafurova N. O.

Republican Specialized Scientific and Practical Medical Center for Maternal and Child Health, Tashkent, Uzbekistan

Abstract Twin-to-twin (feto-fetal) transfusion syndrome is a very dangerous complication that affects approximately 10-15% of monochorionic twin pregnancies. The inter-twin hemodynamic imbalance and its pathogenesis was very well described by the German gynecologist Friedrich Schatz in 1882. According to various studies, the occurrence of at least one arteriovenous anastomosis can cause TTTS. Thus, blood flows through the arterial vessels of the donor to the veins of the recipient in one direction. If there are not enough anastomoses to compensate for this blood flow, an unbalanced redistribution of blood between the two fetuses occurs. Postnatal placental injection studies have identified an important association between the absence of superficial arterio-arterial anastomosis and the development of TTTS. The object of the study was female patients aged 35 and 38 years who came to the Republican Specialized Scientific and Practical Medical Center for Maternal and Child Health, where they were diagnosed with: Pregnancy 24-26 weeks, monochorionic diamniotic twins. Twin-to-twin transfusion syndrome Quintero stages 2-3. Due to the presence of TTTS stages 2-3 at weeks 24-27, it was decided to correct twin-to-twin transfusion syndrome by amnioreduction. Amnioreduction was performed at the Republican Specialized Scientific and Practical Medical Center for Maternal and Child Health. At 31-32 weeks of gestation, emergency premature delivery was performed by cesarean section. Preterm male newborns were born alive. The newborns were given to resuscitation experts and neonatologists to care. The children were treated in the neonatal intensive care unit, later in the neonatal pathology department, and were allowed to go home in satisfactory condition.

Keywords Twin-to-twin transfusion syndrome, Monochorionic diamniotic twins, Pregnancy, Amnioreduction, Prematurity, Donor fetus, Recipient fetus

1. Introduction

Twin births are estimated to account for 2% to 4% of all births worldwide. In the United States, the 2018 twin birth rate was about 33 per 1,000 live births, equivalent to about 3%, according to the National Vital Statistics System of the National Center for Health Statistics of the Centers for Disease Control and Prevention. This is significantly higher than 1.8% in 1980. Among twin pregnancies, about 67% are dizygotic and 33% are monozygotic. Among monozygotic twins, approximately 75% have a monochorionic diamniotic placenta. Twin-to-twin transfusion syndrome occurs in approximately 8-10% of monochorionic diamniotic twin pregnancies and about 6% of monochorionic monoamniotic twin pregnancies. In general, TTTS affects 1 to 3 per 10,000 births. Since in vitro (extracorporeal) fertilization has the potential to give birth to monozygotic twins, such pregnancies may also be complicated by TTTS. There are limited data on the prevalence of each stage of TTTS. According to reference centers, the Society of Maternal-Fetal Medicine (SMFM) estimates the prevalence of stage I to be 11-15%, stage II

20-40%, stage III 38-60%, stage IV 6-7% and stage V — 2%. Twin-to-twin transfusion syndrome is rare, affecting about 15% of monochorionic twins. At the same time, vascular connections are present in almost all monochorionic twins; in most cases, blood flow remains balanced, without significant blood transfusion from one twin to the other. Twin-to-twin transfusion syndrome (also feto-fetal transfusion syndrome) is a condition in which blood flows unevenly between twins who share a placenta (monochorionic twins). In twin-to-twin transfusion syndrome, uneven blood flow between twins sharing a placenta causes the recipient twin (right) to accumulate excess amniotic fluid, while the donor twin (left) has little or no amniotic fluid.

2. Materials of the Study

An analysis of clinical observations of multiple pregnancies complicated by TTTS was carried out.

Serial amnioreduction, the repeated removal of excess amniotic fluid by amniocentesis, is the most accepted treatment.

Clinical case 1. The subject of the study was patient M., 35 years old, came to the Republican Specialized Scientific and Practical Medical Center for Maternal and Child Health,

where she was diagnosed with: Pregnancy 27 weeks 1 day, monochorionic diamniotic twins. Twin- to-twin transfusion syndrome Quintero stages 2-3. Mild anemia in pregnancy. This third pregnancy occurred spontaneously, with a history of two urgent surgical births at full-term gestation. This pregnancy was without any special features. At 17-18 weeks, the pregnant woman suffered an ARI (acute respiratory infection) with an increase in body temperature; she was treated in the maternity hospital, received antibacterial therapy Amoxicillin 1000 mg 2 times a day for 7 days, antiviral therapy Arbidol 200 mg 4 times a day for 5 days, infusion therapy Ascorbic acid with saline solution. Due to the presence of TTTS stages 2-3 at week 27, it was decided to correct twin-to-twin transfusion syndrome by amnioreduction. At the Republican Specialized Scientific and Practical Medical Center for Maternal and Child Health, amnioreduction was performed and 3 liters of amniotic fluid were removed. She was allowed to go home the next day in satisfactory condition under the supervision of an obstetrician-gynecologist. Every 7 days, the pregnant woman underwent ultrasound and Doppler examinations. At 31 weeks 2 days of gestation, the patient began to complain about vaginal bloody discharge, periodic pain in the lower abdomen, and leaking amniotic fluid. A pregnant woman was hospitalized at the Maternal and Child Health Center with a diagnosis: the third pregnancy 31 weeks 2 days, Childbirth 3. Multiple pregnancy. Monochorionic diamniotic twins. Premature prenatal rupture of membranes. Burdened obstetric and gynecological anamnesis (two scars on the uterus). Blood pressure upon examination was 110/70 mmHg. According to laboratory examinations: 1) General blood test - hemoglobin 74 g/l, hemoglobin - 23.0%, platelets 211, leukocytes 7.3, lymphocytes - 11%, monocytes - 2%, ESR - 33 mm/hour. 2) General urine analysis - specific gravity - 1010, protein - 0.08, leukocytes - 2-3, unchanged erythrocytes - 5-7, altered erythrocytes - 0-1. 3) Biochemical blood test - total bilirubin - 11.5 $\mu\text{mol/l}$, total protein - 55.0 g/l, urea - 5.0 mol/l, creatinine - 78.2 $\mu\text{mol/l}$, ALT - 19.0 units /l, AST - 26.0 units/l. 4) Analysis of the blood coagulation system - prothrombin time - 13.5 seconds, PTT - 25.4 seconds, fibrinogen - 4.5 g/l, SFC - 9 mg%, INR - 1.0. Ultrasound and Doppler - Pregnancy monochorionic diamniotic twins 32 weeks 6 days according to LDM, according to fetometry of the first fetus: 32 weeks 3 days, according to fetometry of the second fetus: 31 weeks 5 days. Threat of premature birth. Ventriculomegaly in the second fetus. TTTS docked. Premature prenatal rupture of membranes. Violation of the uteroplacental-fetal circulation in the second fetus, stage 1B. In the hospital, she received prophylaxis for fetal RDS (respiratory distress syndrome) - Dexamethasone 6 mg IM No. 4, antibacterial prophylaxis - erythromycin 500 mg 3 times a day, tocolytic therapy - nifedipine 10 mg according to the scheme, antianemic therapy. At 31 weeks 4 days of gestation, the pregnant woman complained of regular contractions. The diagnosis was made: the third pregnancy 31 weeks 4 days, Childbirth 3. Multiple pregnancy. Monochorionic diamniotic twins. Premature prenatal rupture of membranes. 1st stage of labor. Burdened

obstetric and gynecological anamnesis (two scars on the uterus). Severe anemia. An emergency premature delivery was performed by cesarean section. Intraoperative transfusion of two doses of red blood cells was performed. Live premature newborns were born male, weighing 1581 g, on the Apgar scale 5/7 points, and female, weighing 1920 g, on the Apgar scale 6/7 points. The newborns were given to resuscitation experts and neonatologists to care. The children were treated in the neonatal intensive care unit, later in the neonatal pathology department, and were allowed to go home in satisfactory condition. In the early postpartum period, the patient's condition and laboratory and instrumental examination parameters gradually became normal. In a clinical blood test: leukocytes - $7.0 \times 10^6 / l$, hemoglobin - 103 g/l, color index - 0.9, platelets - $204 \times 10^4 / L$. In the general analysis of urine - specific gravity - 1010, protein - 0.08, leukocytes - 2-3, unchanged erythrocytes - 5-7, altered erythrocytes - 0-1. Biochemical blood test - total bilirubin - 10.5 $\mu\text{mol/l}$, total protein - 59.0 g/l, urea - 5.0 mol/l, creatinine - 78.2 $\mu\text{mol/l}$, ALT - 18.0 units/l, AST - 25.0 units/l.

Clinical case 2. Patient M., 38 years old, came to the Republican Specialized Scientific and Practical Medical Center for Maternal and Child Health, where she was diagnosed with: Pregnancy 24 weeks 1 day. Monochorionic diamniotic twins. Twin- to-twin transfusion syndrome Quintero stage I. Mild anemia in pregnancy. This is the seventh pregnancy, it occurred spontaneously, with a history of two spontaneous miscarriages in the first trimester.

According to echography: Monochorionic diamniotic twins. The size of the fetuses corresponded to the gestation period of 24 weeks. TTTS stage II. Reduction in the volume of amniotic fluid and visualization of the bladder of the donor fetus, polyhydramnios in the recipient fetus (maximum vertical pocket (MVP) – 16 cm). The fetal blood flow of the fetuses is not impaired. Due to the presence of TTTS stages II, it was decided to perform amnioreduction. at the Republican Specialized Scientific and Practical Medical Center for Maternal and Child Health, a total of amnioreduction was performed three times and 3-4 liters of amniotic fluid were removed sequentially (a total amount of 10 liters of amniotic fluid) at gestation periods of 24, 26, 28 weeks, respectively. Magnesium, antibacterial, and tocolytic therapy were carried out. At 30 weeks of gestation, the patient began to complain of swelling in the face, lower and upper extremities, and headache. Blood pressure upon examination was 115/65 mmHg. According to laboratory examinations, there was an increase in anemia (hemoglobin - 68 g/l), hypoproteinemia (total protein - 41.8 g/l), an increase in transaminase titer (ALT - 188.7 U/l, AST - 193.0 U/l). Schizocytes were not detected in a clinical blood test. There was no proteinuria. According to ultrasound examination, swelling of the skin and subcutaneous fat of the head and body of the recipient fetus persisted. Amniotic fluid in the donor fetus shows oligohydramnios (MVP 15 mm), and in the recipient fetus there is polyhydramnios (MVP – 120 mm). According to echography, free fluid was detected in the pleural cavities of the pregnant woman. Transfusion of red

blood cells, antianemic therapy, infusion of 20% albumin solution, and anticoagulant therapy were carried out. At 31 weeks of gestation, emergency premature delivery was performed by cesarean section. Live premature female newborns were born, weighing 1520 g and 1340 g, length 38 cm and 37 cm, respectively, with an Apgar score of 4/6 and 4/6 points, respectively. The children were treated in the neonatal intensive care unit, later in the neonatal pathology department, and were allowed to go home in satisfactory condition. In the early postpartum period, the patient's condition and laboratory and instrumental examination parameters gradually became normal.

3. Results

The average age of patients at the time of intrauterine intervention was 36 years. The patients' gestational age at the time of amniodrainage was 728 ± 17.0 days, with a range of 672 to 756 days. The average amniotic drainage was 3607 ± 1259 ml with the classical technique. The infants' gestational age at birth was 868 ± 28 days and 896 ± 33 days. The average weight of the infants was 1590.25 grams with a range of 1340 to 1920 grams. We found no differences in Apgar values between infants.

4. Discussion

Serial amnioreduction, the sequential removal of excess amniotic fluid through amniocentesis, is the most accepted treatment method. It was originally used to treat polyhydramnios in the recipient sac, to prevent preterm labor, leaking amniotic fluid, or both, but may also have beneficial effects on the condition of disease (Montan 1985; Schneider 1985). Uterine artery color Doppler waveform studies assessing fetal well-being showed the improvement following amnioreduction (Bower 1995). Other authors reported a decrease in the rate of fluid accumulation after serial amnioreduction and therefore an increase in the interval between contractions (Schneider 1985; Urig 1990). They suggest that polyhydramnios compresses the placenta, increasing the rate of blood transfusion to the recipient twin, and reducing this pressure through amnioreduction reverses this process (Urige 1990). On the other hand, an increase in fetoplacental blood volume with increasing gestational age may reduce the effect of anastomoses, indicating an improvement in the condition (Saunders 1991). Regardless of the physiological mechanisms underlying the procedure, amnioreduction appears to prolong pregnancy and therefore improve fetal survival. Survival after serial amnioreduction is estimated to range from 37% to 60% (Saunders 1991; Trespidi 1997; Urig 1990), and the risk of neurological damage ranges from 17% to 33%. Some studies report very high survival rates of about 79% (Elliot 1991; Mahony 1990; Reisner 1993), but the results are controversial due to the failure to exclude pregnancies with non-identical twins or fetuses with structural

abnormalities. The cohort studies included mild cases of TTTS, which may explain the better results. Serial amnioreduction does not require special equipment and can be performed by most obstetricians who specialize in fetal medicine. Procedure-related complications occur in approximately 10% of cases of serial amnioreduction (Mahony 1990; Saunders 1991), most commonly fetal death within 48 hours of the procedure or spontaneous abortion. Cases of placental abruption have also been reported (Mahony 1990; Reisner 1993).

5. Conclusions

The prognosis for the health of the mother and fetus in multiple pregnancies complicated by twin-to-twin transfusion syndrome is usually unfavorable. Without treatment, this condition often leads to the death of one or both fetuses, which is confirmed by our observations. Timely therapy, including amnioreduction and laser coagulation of placental vascular anastomoses, can improve the condition of the fetus, prolong pregnancy and improve the clinical condition of the woman and the outcome for the fetus.

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