Case report

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ACUTE NEONATAL BRAIN INJURY IN TWIN-TO-TWIN TRANSFUSION SYNDROME

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Twin-to-twin transfusion syndrome is a severe complication of monochorionic twins that share one placenta. Studies have shown an increased risk of acute brain injury and long-term poor neurodevelopmental outcome. The most common cerebral lesions are cystic form of periventricular leukomalacia, severe intraventricular hemorrhage and posthemorrhagic ventricular dilatation.

A 30 weeks of gestation, 1120 g female neonate was born by caesarean section from pregnancy complicated by twin-to-twin transfusion syndrome and intrauterine fetal demise of the fetus recipient. Immediately after birth, the neonate was intubated, placed on mechanical ventilation and received a red blood cell transfusion. The cranial ultrasound showed cystic form of periventricular leukomalacia and intracerebral hemorrhage in early neonatal period. The neonate had neonatal seizures, pulmonary hemorrhage and patent ductus arteriosus. The neonate was discharged home in the second month of life with a weight of 2300 g.

Considering the high incidence of acute brain injury, we recommend serial cranial ultrasound examinations and careful neurological follow-up in all surviving neonates with twin-to-twin transfusion syndrome.

Key words: pregnancy, monochorionic twins, twin-twin transfusion syndrome, brain injury, prematurity

Prikaz bolesnika

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AKUTNO NEONATALNO OŠTEĆENJE MOZGA U SINDROMU MEĐUBLIZANAČKE TRANSFUZIJE

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Sindrom međublizanačke transfuzije je teška komplikacija monohorionskih blizanaca koji dele jednu placentu. Studije su pokazale povećan rizik od akutnog oštećenja mozga i dugoročno lošeg neurorazvojnog ishoda. Najčešće moždane lezije su cistična forma periventrikularne leukomalacije, teška intraventrikularna hemoragija i posthemoragijska ventrikularna dilatacija. Novorođenče ženskog pola, porođaje telesne mase 1120 g, rođeno je carskim rezom u 30. nedelji gestacije iz trudnoće komplikovane sindromom međublizanačke transfuzije i intrauterusnom smrću fetusa primaoca. Neposredno po rođenju, novorođenče je intubirano, primenjena je mehanička ventilacija i primilo je transfuziju eritrocita. Ultrazvuk glave pokazao je cističnu formu periventrikularne leukomalacije i intracerebralno krvarenje. Novorođenče je imalo neonatalne konvulzije, plućnu hemoragiju i otvoren arterijski kanal. Novorođenče je otpušteno kući u drugom mesecu života, sa telesnom masom 2300 g.

S obzirom na visoku učestalost akutnog oštećenja mozga, preporučujemo serijske ultrazvučne preglede glave i pažljivo neurološko praćenje sve preživele novorođenčadi sa sindromom međublizanačke transfuzije.

Ključne reči: trudnoća, monohorionski blizanci, sindrom međublizanačke transfuzije, oštećenje mozga, prematuritet

Introduction

Twin-to-twin transfusion syndrome (TTTS) is a severe complication of monochorionic twins that share one placenta. Its serious and potentially lethal condition where blood passes from one twin to the other, leading to an imbalance in blood flow through placental vascular anastomoses. The fetus recipient gains too much fluid, leading to polyhydramnios and polycythemia, while the fetus donor loses fluid, leading to oligohydramnios, fetal growth restriction (FGR) and frequently, anemia. Pregnancy complicated by TTTS often ends in premature birth (1, 2).

Multisystemic complications, including neurological, cardiovascular, renal, and hematological, are common in surviving twins with TTTS. Several studies have shown an increased risk of acute brain injury and long-term poor neurodevelopmental outcome in twins with TTTS, especially those born prematurely. The most common neurological complications of TTTS are cystic form of periventricular leukomalacia (PVL), severe intraventricular hemorrhage (grade III and IV) and subsequent posthemorrhagic ventricular dilatation (PHVD). Other neurological complications that may occur in these neonates are arterial ischemic stroke and cerebral atrophy (3, 4). Minor cerebral lesions associated with monochorionic twin pregnancy complicated with TTTS are subependymal pseudocysts and lenticostriate vasculopathy (3 ,5). The optimal neuroimaging for diagnosing acute brain injury in the neonatal intensive care unit (NICU), especially when the neonate is hemodynamically and respiratory unstable, is cranial ultrasound (CUS). We report a case of the preterm neonate with acute brain injury as a complication of TTTS.

Case report

A 30 weeks of gestation, 1120 g female neonate was born by caesarean section to a 37-year-old mother from the first controlled twin pregnancy. Apgar scores were 4 and 6 in the first and five minute after birth, respectively. A monochorionic diamniotic twin pregnancy was conceived through in-vitro fertilization, complicated by TTTS (Quintero Stage V) and intrauterine fetal demise (IUFD) of the fetus recipient just before delivery. A septostomy was performed at 20 weeks of gestation. Immediately after birth, the neonate was intubated, placed on mechanical ventilation (MV) and surfactant was administered. Also, the neonate received dual antibiotic therapy (ampicillin and amikacin), methylxanthine preparation (caffeine) and total parenteral nutrition. Due to anemia at birth, the neonate received a red blood cell (RBC) transfusion.

After initial stabilization in the Maternity Ward, the neonate was admitted to the NICU of our hospital on the second day of life (DOL) in severe condition, so MV and antimicrobial therapy was

continued. After admission at NICU, the neonate had seizures, stopped after the neonate received loading dose of phenobarbital, followed by daily maintenance doses. Neurologically, the neonate had generalized hypotonia, primitive reflexes and deep tendon reflexes were weakened. The CUS performed at second DOL showed bilateral periventricular fronto-parieto-occipital patchy hyperechoic changes with cysts formation (Figure 1). The following day, CUS showed subependymal hemorrhage with bilateral frontal periventricular intracerebral hemorrhage (ICH), larger on the left side, as well as the cystic form of PVL (Figure 2). The size of the brain ventricles was normal at all times. The neonate was hemodynamically unstable, so inotropic support was started. The course of hospitalization was complicated by the development of pulmonary hemorrhage due to a hemodynamically significant patent ductus arteriosus (PDA) closed with paracetamol. Also, in the further course, the neonate had refractory neonatal seizures, which were stopped by the administration of midazolam in continuous intravenous infusion. After stabilization, interictal video electroencephalography (EEG) recording was performed and showed irregularity of the basic activity without epileptic discharges. During control CUS, gradual reduction of ICH was registered with cystic form of PVL and porencephalic cyst in left frontal periventricular region (Figure 3). Hypotonia and hyporeflexia persisted during hospitalization, without focal neurological signs. Control video EEG recording showed no epileptic discharges and the neonate had no repeated clinical signs of seizures, so antiseizure medications was gradually discontinued.

The neonate was discharged home in the second month of life (corrected 39 weeks of gestation) with a weight of 2300 g (less than the 10th percentile for the gestational age). Neurologically, the neonate had no facial asymmetry, truncal muscle hypotonia and mild extremities muscle hypertonia, deep tendon reflexes are present in the arms and legs, Moro reflex performed spontaneously with normal sucking and swallowing. The neonate required further follow-up with a pediatric neurologist and physiatrist after discharge from our hospital.

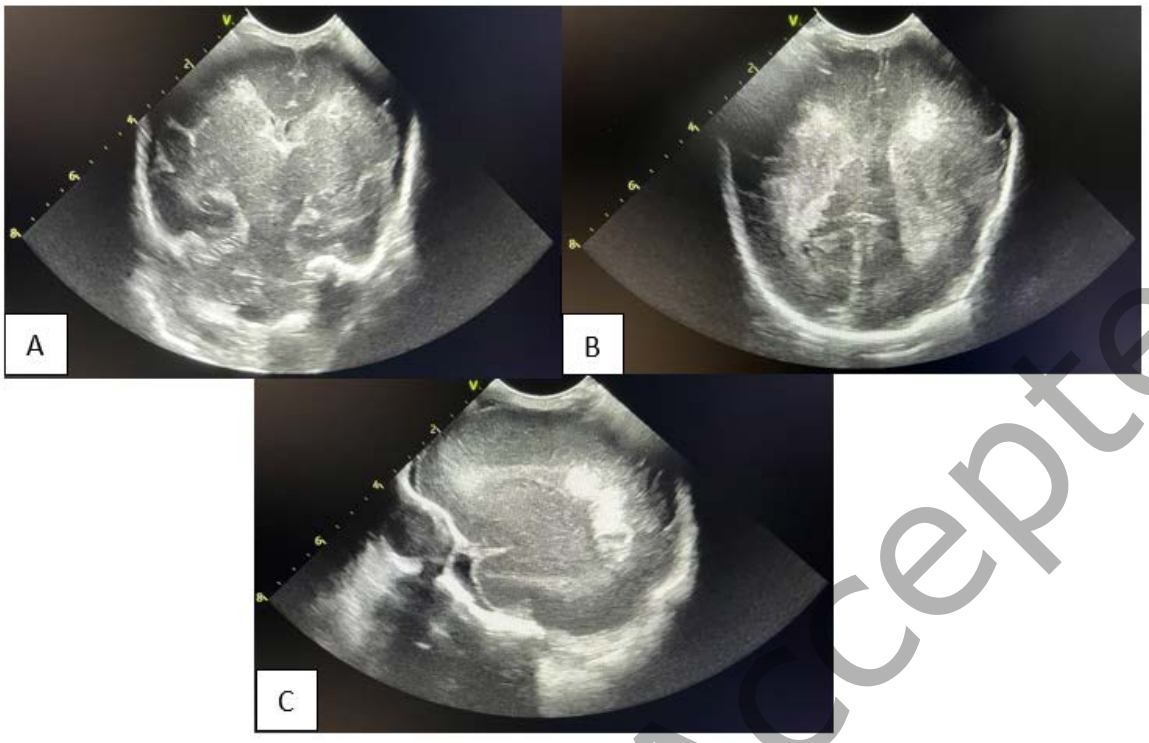

Figure 1. Bilateral periventricular fronto-parieto-occipital patchy hyperechoic changes with cysts formation: A and B– coronal plane, C – left sagital plane.

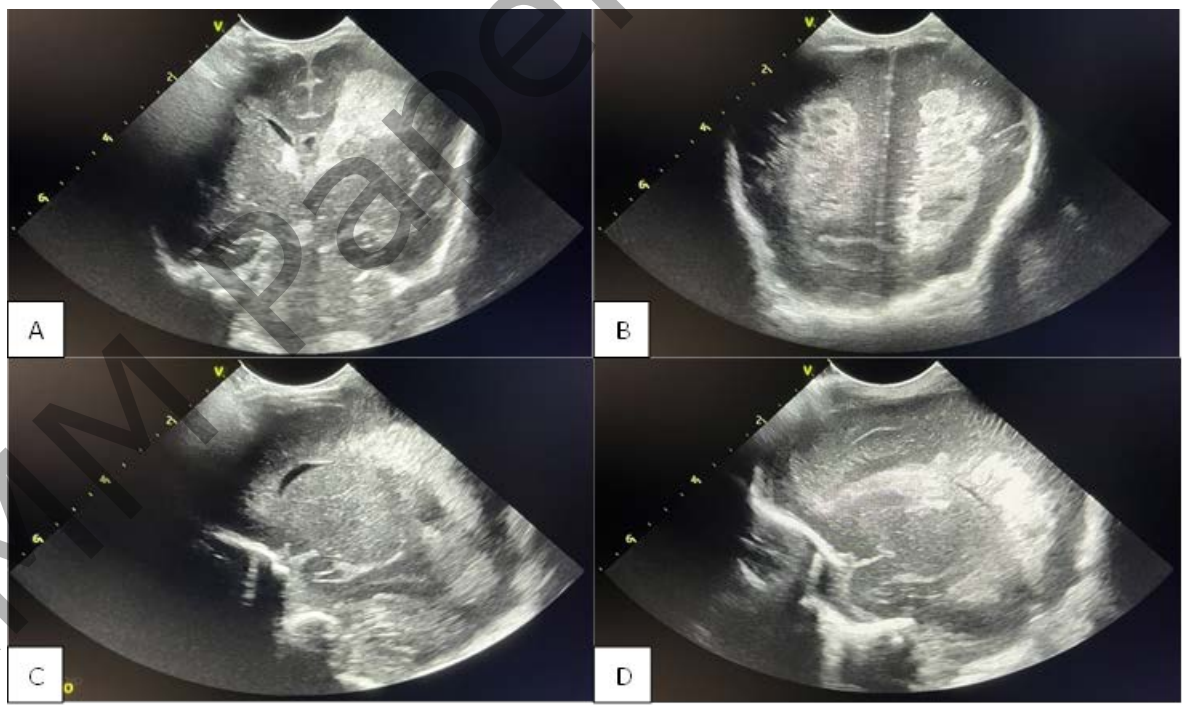

Figure 2. Subependymal hemorrhage with bilateral frontal periventricular intracerebral hemorrhage, larger on the left side, as well as the cystic form of periventricular leukomalacia: A and B – coronal plane, C – right sagital plane, D – left sagital plane

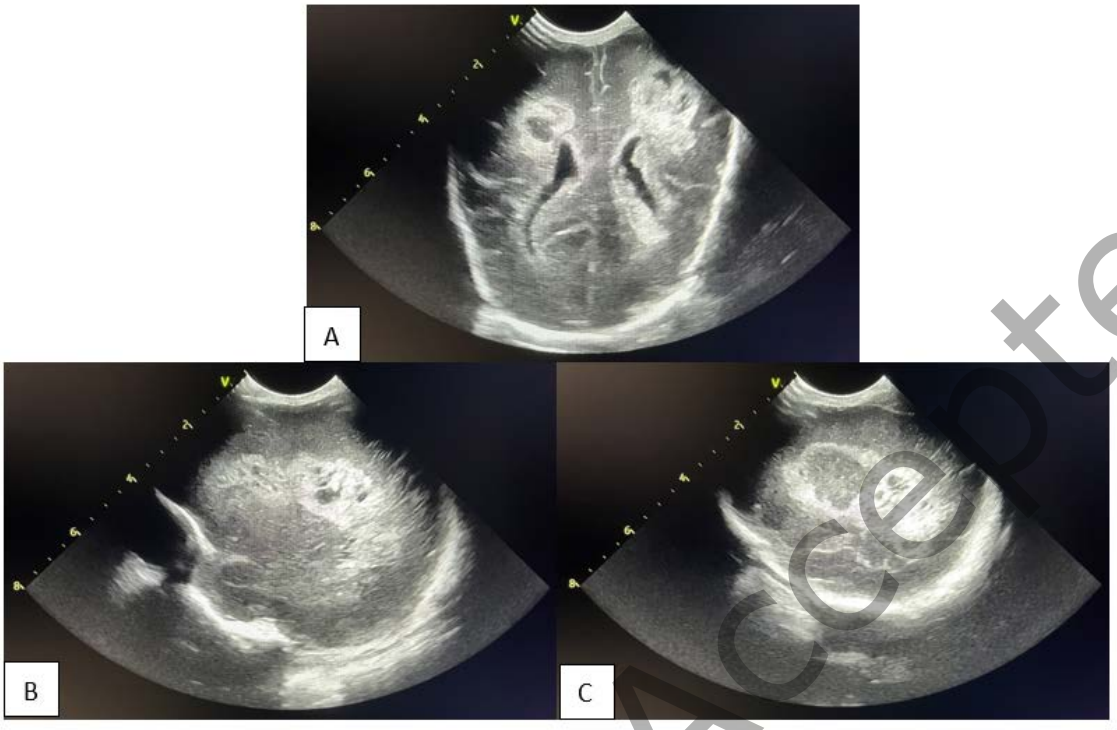

Figure 3. A gradual reduction of intracerebral hemorrhage with cystic form of periventricular leukomalacia and formation of porencephalic cyst, more pronounced in left frontal periventricular region: A – coronal plane, B – right sagital plane, C – left sagital plane

Discussion

We presented female preterm neonate who survived from monochorionic twin pregnancy complicated with TTTS and had severe brain lesions diagnosed by CUS in early neonatal period. It is estimated that TTTS occur in 10-15% of monochorionic twin pregnancies. Studies have shown that TTTS is associated with an increased risk of fetal/neonatal death and neonatal mortality ranges from 5 to 29%. Mortality in the neonatal period is higher when TTTS is treated with amnioreduction (14-29%), compared to fetoscopic laser photocoagulation (5-8%) (1, 6-8).

Cerebral lesions as a complication of TTTS can occur antenatal and postnatal. In addition to being a consequence of TTTS itself, cerebral lesions can also be associated with preterm birth. The pathogenesis of brain injury in TTTS is not completely understood. Cerebral hypoperfusion and hemodynamic disturbances in cerebral circulation can lead to antenatal brain injury. Brain injuries that occur postnatally are usually associated with prematurity and low birth weight (3, 5, 6). Jiang T et al. conducted a retrospective cohort study and showed that invasive MV, necrotizing

enterocolitis, single IUFD and Apgar score < 9 at fifth minute after birth are independent risk factors for brain injury in preterm neonates with TTTS (4). In perinatal history of our case, there were well-known risk factors for brain injury in TTTS, such as prematurity, very low birth weight, Apgar score of 6 at fifth minute after birth, single IUFD and use of MV. Cranial ultrasound detected periventricular leukomalacia as early as at the first examination, on the second day of life, indicating intrauterine onset of brain injury.

Severe intraventricular hemorrhage (IVH) in neonates with TTTS usually occur in recipient twins as a result of significant, unequal levels of hemoglobin between two fetuses in a monochorionic twin pregnancy and polycythemia. However, IVH can also occur in donor twins, as in our case, which may be due to blood pressure instability and hypotension (9). Our case was very preterm neonate, born between 28 and less than 32 weeks of gestation, had a hemodynamically significant PDA and required the use of inotropic support. Cases of IVH and consequent PHVD in donor twins in monochorionic twin pregnancy complicated with TTTS have been described in the literature (10).

The introduction and use of laser surgery in the treatment of TTTS significantly increased the survival of these neonates, who are often born prematurely. At the same time, long-term complications are common in surviving neonates (11). Numerous studies have shown in surviving neonates the existence of long-term neurodevelopmental disabilities, including motor and/or congitive developmental delay, as well as vision and hearing impairment. It is estimated that about 20% of infants with TTTS have neurodevelopmental disorders. The incidence and type of long-term neurodevelopmental disabilities depend on the method of prenatal treatment of TTTS, neonatal management, and the presence and type of cerebral lesions (3, 11, 12).

Conclusion

Twin-to-twin transfusion syndrome is associated with an increased risk for fetal/neonatal death, numerous acute complication and poor neurodevelopmental outcome in surviving neonates. Given the high incidence of acute cerebral lesions, we recommend serial CUS examinations and careful neurological follow-up in all surviving neonates with TTTS. Due to the risk of preterm birth and to ensure optimal obstetric and neonatal care and management, transport of a pregnant woman whose pregnancy is complicated by TTTS to a tertiary Maternity Ward is required.

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