CASE REPORT

Two intrauterine rescue transfusions in treatment of severe fetomaternal hemorrhage in the early third trimester

Vedran Stefanovic, Jorma Paavonen, Erja Halmesmäki, Päivi Luukkainen, Minna Tikkanen, Mika Nuutila & Piia Poikkeus

1Department of Obstetrics and Gynecology, Helsinki University Central Hospital, Helsinki, Finland
2Hospital For Children and Adolescents and Department of Pediatrics, Helsinki University Central Hospital, Helsinki, Finland

Correspondence
Vedran Stefanovic, Department of Obstetrics and Gynecology, Helsinki University Central Hospital, P.O. Box 140, 00029 HUS, Finland.
Tel: + 350 40 760 5581; Fax: + 358 9 4717 4902; E-mail: vedran.stefanovic@hus.fi

Key Clinical Message
When massive fetomaternal hemorrhage is diagnosed in the early third trimester of pregnancy, serial fetal intravascular transfusion may be an alternative to immediate delivery.

Keywords
Fetomaternal hemorrhage, intrauterine transfusion, preterm birth.

Introduction
FMH is a physiological event most often associated with small volumes of blood transferred across the placenta before or during delivery [1] with an estimated incidence of 0.3% [2, 3]. Usually such small volumes are of no fetal importance but FMH may lead to alloimmunization of Rh (D)-negative mothers. Severe FMH (involving volumes greater than 30 mL) can result in adverse pregnancy outcome (stillbirth, neonatal death, cerebral palsy, and other neurological damage) [1]. Many cases of mild FMH remain undetected or undiagnosed. If severe FMH is diagnosed antenatally at second or early third trimester, cordocentesis with intrauterine intravascular transfusion (IUT) should be considered as standard management for pregnancy prolongation [1]. We describe a case with massive persistent FMH with two consecutive successful IUTs.

Case Presentation
A 34-year-old primigravida was admitted to our tertiary referral hospital at 27 + 1 gestational weeks after 2 days history of decreased fetal movements. She conceived by in vitro fertilization and the pregnancy course has been unremarkable with two normal screening ultrasound scans at 12 and at 20 weeks of gestation. Her blood group was AB, Rh-positive with no detectable blood group antibodies. At presentation, clinical examination revealed closed cervix and soft uterus without vaginal bleeding. The fetus was in cephalic presentation with an estimated weight of 1050 g (appropriate for gestational age). The umbilical artery Doppler flow velocimetry was normal, two limb and two gross body movements were seen within 10 min. The fetal heart rate (FHR) was 140 beats per min. A typical sinusoidal cardiotocography (CTG) pattern appeared with some variable decelerations observed after admission (Fig. 1). Antenatal steroids were administered for acceleration of fetal lung maturation.

The next ultrasonographic examination performed by the experienced perinatologist revealed increased peak systolic velocity (PSV) of 55 cm/sec (1.55 MoM [Multiples of Median]) in the middle cerebral artery (MCA), absence of fetal movements, decreased amount of amniotic fluid, but no fetal hydrops. The ultrasound findings and the increased concentration of fetal hemoglobin (HbF) in maternal circulation (3%, assessed with high pressure liquid chromatography method) raised the suspicion of
severe FMH. Also, the patient’s blood group analysis showed signs of second type of red cells suggestive of FMH. Maternal viral antibodies showed old immunity to parvovirus.

The first IUT was performed 12 h after admission at 27 + 2 gestational weeks. The initial umbilical vein hemoglobin concentration was 18 g/L. The hemoglobin increased to 119 g/L after transfusion of 35 mL of O, Rh-negative red blood concentrate into the umbilical vein. After IUT, fetal movements returned to normal. Also, the sinusoidal FHR pattern disappeared and changed into normal FHR pattern (Fig. 2). However, at 27 + 6 gestational weeks, the fetal movements decreased again and the next day an intermittent sinusoidal CTG pattern reappeared. The PSV of MCA dramatically increased to 77 cm/sec (>1.55 MoM). These clinical findings were consistent to recurrent FMH and led to second IUT at 28 weeks of gestation. At this time a transfusion of 40 mL of blood into the umbilical vein yielded an increase in hemoglobin concentration from 32 to 105 g/L (Table 1).

As severe FMH and fetal anemia reoccurred soon after the first IUT, the risk of massive FMH and ultimately stillbirth was considered. After consulting the neonatologist, an elective cesarean section was performed. A female child (weight 1060 g, 1-min Apgar score 3, umbilical artery pH 7.22 and base excess – 2.2) was delivered at 28 + 2 gestational weeks. The newborn was intubated at 1 min age and surfactant was given after 3 min. The umbilical vein hemoglobin concentration was 60 g/L and the first postnatal blood transfusion (20 mL) was performed 3 min after birth.

The neonate was extubated after 6 h. At the first postnatal day, hemorrhagic-ischemic area in the right temporal area was revealed by transfontanellar ultrasonography consistent with antenatal stroke. By 2 weeks this area

Figure 1. Sinusoidal cardiotocography pattern before the first intrauterine intravascular transfusion at gestational weeks 27 + 2.

Figure 2. Normal cardiotocography after the first intrauterine intravascular transfusion at gestational weeks 27 + 2.
began less prominent. The neonate showed no neurological symptoms during the stay at the neonatal intensive care unit (NICU). Three additional blood transfusions at the NICU were required (first postnatal day, and after 1 and 2 weeks). The infant was transferred to a local hospital at the age of 16 days because of prematurity. Presently, at the age of 2 years, neurodevelopment outcome is within normal range.

Histopathologic examination of the placenta revealed remarkable variation in the morphology and maturation of the chorionic villi with mild hypoxic changes but no neoplastic features. A few vessels contained immature nucleated red cells consistent with FMH.

Discussion

We present a case with massive persistent FMH with two emergency IUTs performed only 5 days apart. Presenting symptoms and findings were characteristic of massive FMH including a history of decreased fetal movements, sinusoidal CTG and high peak velocity in MCA. Sinusoidal fetal heart rate pattern was first temporary, then became continuous, and finally disappeared after the first IUT. The sinusoidal pattern reappeared soon thereafter due to persistent FMH. High level of maternal HbF (3%) was in line with the severe fetal anemia confirmed by cordocentesis.

According to a recent comprehensive review [1], only 13 cases of cordocentesis with intrauterine transfusion for massive FMH during the third trimester have been reported. Six of those cases presented with hydrops, six with decreased fetal movements, and one case was identified by a positive Kleihauer-Betke test. The initial fetal hemoglobin concentration ranged from 22 to 88 g/L and all underwent at least one IUT (median 2, range 1–5) with the median of transfused volume of 65 mL (range 26–185 mL). Two fetuses were delivered the same day as the initial IUT was performed and another two within the first week. Delivery was delayed by more than 1 week in the remaining cases (range 2–17 weeks), although additional IUTs were required in some cases.

In our case, the initial fetal hemoglobin concentration was only 18 g/L which is the lowest initial hemoglobin concentration ever reported in FMH cases managed by IUTs. Previously, short- and long-term adverse outcome of anemic fetuses have been associated with fetal hemoglobin concentration of ≤40 g/L [4] and with the volume of FMH ≥20 mL/kg³. In our case, an antenatal stroke without neurological signs was observed by the age of 8 weeks. The clinical suspicion of FMH led to IUT soon after the admission. The repeated IUT’s enabled administration of a full course of antenatal steroids for acceleration of fetal lung maturation, and postponed delivery by 8 days. The diagnosis of fetal anemia after one IUT relies again on clinical symptoms but a higher cutoff level of the PSV of MCA may be used [5]. In our case, higher PSV of MCA was observed before the second IUT although the fetal hemoglobin concentration was higher than that before the first IUT. Due to the recurrence of severe anemia and potential risks associated with IUT, we decided to perform an elective cesarean section after the second IUT at 28 + 2 gestational weeks. Although some guidelines in managing FMH exist [1], a clinician must consider the risks of severe FMH and the risks associated with prematurity. Especially in early third trimester, the optimal treatment requires good antenatal and neonatal facilities. Furthermore, the histological evaluation of the placenta is advisable in cases of severe FMH to exclude placental malignancy [6].

Many factors increase the risk of FMH, such as amnioncentesis, cordocentesis, external cephalic version, monochorionic-monoamniotic twin pregnancy, preeclampsia, abdominal trauma, placental abruption, manual removal of the placenta, and placental tumors [1]. However, the actual cause of FMH remains often unknown as in the presented case.

The management of massive FMH in early third trimester is extremely challenging and requires a close cooperation of obstetrician and neonatologist. We conclude that emergency IUTs in the perinatal centers with high expertise and ability of handling very premature newborns can be used to postpone delivery in cases of massive FMH in such cases.

Conclusions

Intrauterine intravascular transfusion should be performed to correct fetal anemia caused by massive FMH in...
very premature fetuses. The IUT may postpone delivery and thus decrease the risks associated with prematurity. However, FMH may persist and require immediate delivery. In our case, repeat transfusions postponed very preterm delivery by 8 days.

**Conflict of Interest**

Authors declare no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

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