RESEARCH PAPER

Severe Anemia at Birth Due to Massive Fetomaternal Hemorrhage: Report of Two Neonatal Cases With Adverse Neurological Outcome and the diagnostic and treatment challenges in a low-resource setting

Evelina Kreko[1]*Blerina Saraçi Qirinxhi2

[1]*Neonatology Service, University Hospital of Obstetrics and Gynecology "Koço Gliozheni", Tirana, Albania
2. Radiology Service,University Hospital Center "Mother Thereza",Tirana,Albania

Abstract

Background: Fetomaternal hemorrhage (FMH) is an uncommon but potentially devastating obstetric condition caused by the transfer of fetal blood into the maternal circulation. When massive, FMH may result in severe fetal anemia, hypoxic–ischemic injury, multiorgan failure, or stillbirth. Antenatal diagnosis is difficult because clinical manifestations are often subtle.

Objective: To describe two severe neonatal cases of massive FMH presenting with profound anemia at birth and poor neurological outcome,and the diagnostic tools used to determine the cause .

Cases: Both term neonates presented immediately after birth with extreme pallor, metabolic acidosis, and circulatory collapse. Laboratory investigations revealed critically low hemoglobin concentrations (3.1 g/dL and 5.4 g/dL). Intensive resuscitation, mechanical ventilation, and repeated blood transfusions were required. Diagnosis of FMH was confirmed by detection of elevated fetal hemoglobin in maternal blood using flow cytometry and hemoglobin electrophoresis, both performed privately by the patients as they can not be performed in our hospital together with the Kleihauer Betke test. Despite aggressive management, both infants developed hypoxic–ischemic encephalopathy with significant brain injury.

Conclusion: Massive FMH remains a rare but life-threatening cause of severe neonatal anemia. Decreased fetal movements may be the only antenatal warning sign. Early suspicion, rapid diagnosis, and immediate neonatal intervention are essential; however, neurological prognosis remains guarded in severe cases.

Keywords: fetomaternal hemorrhage; severe neonatal anemia; hypoxic–ischemic encephalopathy; fetal anemia; neurological outcome

How to cite this article: Kreko E, Qirinxhi BS. Severe Anemia at Birth Due to Massive Fetomaternal Hemorrhage: Report of Two Neonatal Cases With Adverse Neurological Outcome and the Diagnostic and Treatment Challenges in a Low-Resource Setting. Int J Drug Deliv Technol. 2026;16(30s):242-246. DOI: 10.25258/ijddt.16.30s.25

Introduction

Fetomaternal hemorrhage (FMH) is defined as the passage of fetal blood into the maternal circulation before or during delivery. Antenatal fetomaternal hemorrhage is a pathological condition with a wide spectrum of clinical variation .Small-volume transplacental bleeding occurs physiologically in most pregnancies; however, large-volume hemorrhage may have catastrophic fetal and neonatal consequences[1,2]. Clinically significant FMH is estimated to occur in approximately 1 in 1,000–5,000 pregnancies, while massive FMH is considerably rarer[1]. Secondary fetal anemia may lead to decreased oxygen delivery, metabolic acidosis, cardiovascular collapse, neurological injury, or intrauterine fetal demise[2,7].The vast majority of spontaneous FMHs are low-volume bleedings with no hemodynamic significance but can cause alloimmunization[1]. The frequency and volume of these types of transfusions increase with advancing gestational age, reaching a peak at birth [2]. There is no universally accepted threshold to establish fetal erythrocytes volume in maternal circulation to define a small versus massive FMH. Although volumes of up to 150 mL have been proposed to define massive FMH [1,2], the volume of bleeding should be interpreted in relation to total fetoplacental blood volume, which correlates with fetal size and gestational age.

Recognition of FMH is challenging because antenatal signs are nonspecific. The most frequently reported symptom is reduced fetal movements[3.4], while cardiotocography and ultrasound findings may remain normal. Diagnosis is often made only after birth when the newborn presents with unexplained severe anemia.

The Kleihauer–Betke test has traditionally been used for diagnosis but has limited sensitivity[5]. Flow cytometry is currently considered the gold standard for accurate quantification of fetal erythrocytes in maternal blood.

We present two severe neonatal cases of massive FMH with unfavorable neurological outcome to highlight diagnostic difficulties in a low resource setting as ours , management strategies, and prognostic implications.

Case Reports

Case 1

A female neonate was delivered at 39 weeks of gestation by planned cesarean section to a G2P1 mother. Pregnancy had been uneventful until two days prior to delivery, when the mother noticed decreased fetal movements,refered after the delivery when she was asked a detailed pregnancy history.There was no

*Author for Correspondence: Evelina Kreko

history of trauma, vaginal bleeding, abdominal pain, or infection. The mother was Rh positive.

Birth weight was 3,300 g. At delivery, the newborn was extremely pale(Fig 1) with severe respiratory depression. Apgar scores were 4 and 2 at 1 and 5 minutes, respectively. Bag–mask ventilation was ineffective, and the infant was immediately intubated.

Umbilical cord blood gas analysis showed severe acidosis (pH 7.03, lactate 11.5 mmol/L). On admission to the neonatal intensive care unit (NICU), laboratory evaluation revealed profound anemia: hemoglobin 3.1 g/dL, hematocrit 9.4%, and erythrocytes 0.8 × 10^6/mm^3. Platelet count was 27,000/mm^3.

Arterial blood gases demonstrated persistent metabolic acidosis (pH 7.07, HCO_3^- 7 mmol/L, base excess −24 mmol/L, lactate 20 mmol/L). No signs of hydrops fetalis were present.

Immediate management included volume resuscitation, sodium bicarbonate infusion, fresh frozen plasma, 5% human albumin, and emergency packed red blood cell transfusion, repeated after 12 hours. Inotropic support with dopamine and dobutamine was required for hypovolemic shock.

Parameters	HB	Htc	RBC	Plt
Cord blood	3.1	9.4%	0.8x106	270000
36h	11.2	33%	3,69x106	64000

3 doses of MgSO4 25% as neuroprotective in cases of severe asphyxia are administered, as cooling and continuous neuromonitoring can not be performed in our neonatal intensive care unit.

At 38 hours of life, seizures developed and were treated with phenobarbital. Cranial ultrasound demonstrated grade III–IV intraventricular hemorrhage.(Fig 2,Fig3) Coagulation studies were abnormal (INR 2.0), necessitating vitamin K and plasma administration.

Infectious evaluation, including blood cultures, TORCH screening, and parvovirus serology, was negative. Direct Coombs test was negative, and reticulocyte count was normal.

Flow cytometry performed on maternal blood on day 5 revealed 49‰ fetal hemoglobin, confirming massive FMH. The infant was extubated on day 5 and discharged after 17 days. Neuroimaging showed cerebral parenchymal injury and ventricular dilatation, indicating poor neurological prognosis.

Case 2

A male neonate was born at 40+5 weeks of gestation to a primigravida mother with β-thalassemia minor. Emergency cesarean section was performed due to fetal distress and meconium-stained amniotic fluid.

At birth, the infant was profoundly depressed (Apgar score 1 at 1 minute), hypotonic, and markedly pale. Immediate endotracheal suctioning and intubation were required.

Initial diagnoses included severe perinatal asphyxia with meconium aspiration syndrome(Fig 4), suspected neonatal sepsis, and severe anemia suggestive of FMH.

Laboratory investigations revealed hemoglobin 5.4 g/dL, hematocrit 15.9%, severe metabolic acidosis (pH 6.96, base excess −25 mmol/L, lactate 16 mmol/L), marked leukocytosis (21,800/mm^3), elevated inflammatory markers as CRP and negative Coombs testing.

The neonate required mechanical ventilation with 100% oxygen, surfactant therapy, repeated sodium bicarbonate boluses, packed red blood cell and plasma transfusions, and broad-spectrum antibiotics (ampicillin,gentamycin and imipenem).

On the second day of life, frequent tonic–clonic seizures developed, consistent with hypoxic–ischemic encephalopathy grade II–III, treated with phenobarbital and midazolam .Progressive multiorgan dysfunction ensued, including hepatosplenomegaly, acute kidney injury, hypotension, and generalized edema.

High levels of AST,ALT,creatinin and azotemia gradualy turned into normal ranges in the days to follow.

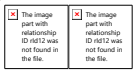
Blood and urine and cerebrospinal liquid culture results were negative.

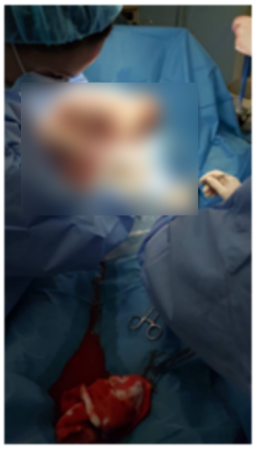
Head computed tomography demonstrated bilateral occipital ischemic lesions and periventricular leukomalacia.

Comparison of maternal hemoglobin electrophoresis before and after delivery revealed a 4.5% increase in fetal hemoglobin, confirming massive FMH. The infant was extubated on day 6 but remained with severe neurological impairment.

Figures

Figure 1. Goast appearance at birth of newborn (Case 1)with FM transfusion





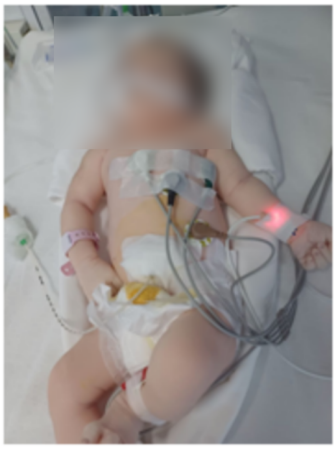
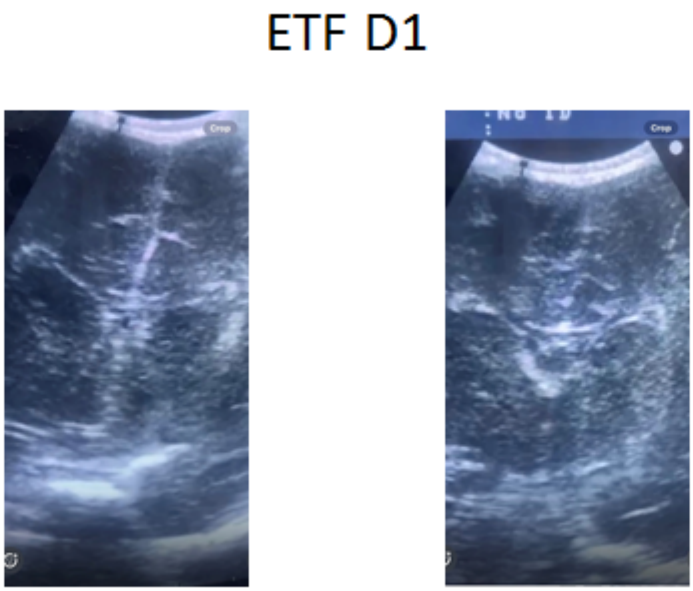


Figure 2. and 3 Cranial ultrasound (Case 1) demonstrating grade III–IV intraventricular hemorrhage with ventricular dilatation.



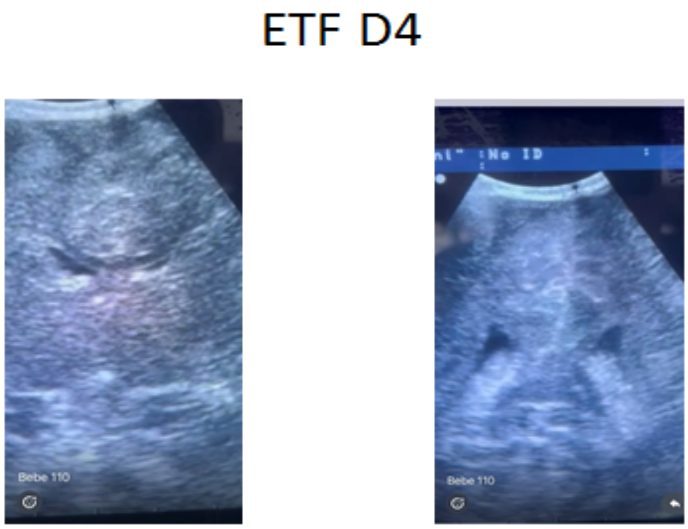
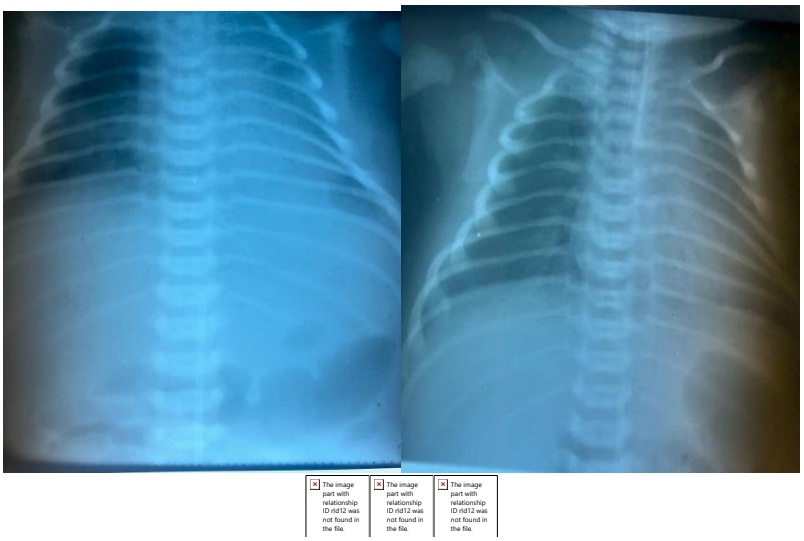


Figure 4. Chest radiograph (Case 2) demonstrating bilateral infiltrates consistent with meconium aspiration syndrome and pneumonia before and after surfactant administratin.



Discussion

Massive fetomaternal hemorrhage represents one of the most dramatic causes of severe neonatal anemia. The clinical severity depends on the volume and rate of fetal blood loss. Acute hemorrhage often results in sudden hypovolemia and profound asphyxia, whereas chronic bleeding may present with compensated anemia[2,6].

Both infants in this report presented with extremely low hemoglobin levels and severe metabolic acidosis, reflecting acute massive hemorrhage. In both cases, decreased fetal movements were retrospectively identified as the only antenatal warning sign,consistent with previous reports[3,4].While in the first case it was a planed cesarean section , and there were no indices of fetal depression in utero ,the second case the baby suffered a severe asphyxia at birth related also because of the meconium aspiration syndrome and probably an in utero infection that complicated the situation and leading to an emenrgency cesarean section.Both cases needed therapeutic hypothermia and continuous neuromonitoring , in order to improve the neurological outcome, but they both are not provided by hospitals in Albania.On the other hand to confirm the diagnosis of FM transfusion in the situation of lacking the standart Kleihaur Betke test and Flow cytometry in our hospital, the first patient preformed it in a private clinique abroad, while for the second mother the comparison of two tests of Hemoglobin electroforesis before and after birth , where the presence of Fetal hemoglobin after birth consisted in a 4,5% rise played an important role in determining the diagnosis.Without their close colaboration it would have been impossibile for us to confirm the diagnosis of FM transfusion.

Early diagnosis remains difficult. Routine cardiotocography and ultrasound may fail to detect FMH[3]. Flow cytometry remains the most reliable diagnostic method and should be considered whenever severe unexplained neonatal anemia is present.

Historically, the Kleihauer–Betke test has been widely used, although it has limitations in sensitivity and accuracy [5]. Alternative methods, such as measurement of maternal alpha-fetoprotein or hemoglobin electrophoresis, may provide supportive diagnostic information [5,13].

Massive FMH has also been implicated in cases of unexplained stillbirth and severe neonatal compromise [8,10]. Long-term outcomes are often poor, particularly when diagnosis and intervention are delayed [9].

Immediate management includes rapid restoration of circulating volume, correction of acidosis, respiratory stabilization, and seizure control. Despite optimal intensive care, neurological injury remains common, as illustrated by both cases.

These findings underscore the importance of heightened obstetric awareness, prompt investigation of reduced fetal movements, and close collaboration between obstetric and neonatal teams.

Conclusion

Massive fetomaternal hemorrhage is a rare but life-threatening condition and an important cause of severe anemia at birth. Decreased fetal movements may be the only antenatal clue[3,4]. Early suspicion, rapid diagnosis, and aggressive neonatal management are essential; however, neurological outcome is often poor in severe cases,particulary in low resource settings[9]. Increased awareness and timely intervention remain crucial to improving neonatal prognosis.

Improvements in the neonatal logistic in Albania are necessary to have better outcome not only in the neonatal mortality, but in the neurological lifelong morbidity of these infants also.

References

1. Sebring ES, Polesky HF. Fetomaternal hemorrhage: incidence, risk factors, time of occurrence, and clinical effects. Transfusion 1990. May;30(4):344-357 10.1046/j.1537-2995.1990.30490273444.x [DOI] [PubMed] [Google Scholar]
2. Giacoia GP. Severe fetomaternal hemorrhage: a review. Obstet Gynecol Surv 1997. Jun;52(6):372-380 10.1097/00006254-199706000-00022 [DOI] [PubMed] [Google Scholar
3. Kosasa TS, Ebesugawa I, Nakayama RT, Hale RW. Massive fetomaternal hemorrhage preceded by decreased fetal movement and a nonreactive fetal heart rate pattern. Obstet Gynecol 1993. Oct;82(4 Pt 2)(Suppl):711-714 10.1097/00006250-199310000-00059 [DOI] [PubMed] [Google Scholar]
4. Heise RH, Van Winter JT, Ogburn PL., Jr Identification of acute transplacental hemorrhage in a low-risk patient as a result of daily counting of fetal movements. Mayo Clin Proc 1993. Sep;68(9):892-894 [DOI] [PubMed] [Google Scholar]
5. Katiyar R, Kriplani A, Agarwal N, Bhatla N, Kabra M. Detection of fetomaternal hemorrhage following chorionic villus sampling by Kleihauer Betke test and rise in maternal serum alpha feto protein. Prenat Diagn 2007. Feb;27(2):139-142 10.1002/pd.1632 [DOI] [PubMed] [Google Scholar]
6. de Almeida V, Bowman JM. Massive fetomaternal hemorrhage: Manitoba experience. Obstet Gynecol 1994. Mar;83(3):323-328 [PubMed] [Google Scholar]
7. Fliegner JR, Fortune DW, Barrie JU. Occult fetomaternal haemorrhage as a cause of fetal mortality and morbidity. Aust N Z J Obstet Gynaecol 1987. May;27(2):158-161 10.1111/j.1479-828X.1987.tb00971.x [DOI] [PubMed] [Google Scholar]
8. Pauli RM. Fetomaternal hemorrhage and still birth. Newsletter of Wisconsin Still birth service program, 1993 Vol 1, N.3. [Google Scholar]
9. Rubod C, Deruelle P, Le Goueff F, Tunez V, Fournier M, Subtil D. Long-term prognosis for infants after massive fetomaternal hemorrhage. Obstet Gynecol 2007. Aug;110(2 Pt 1):256-260 10.1097/01.AOG.0000271212.66040.70 [DOI] [PubMed] [Google Scholar]
10. Laube DW, Schauberger CW. Fetomaternal bleeding as a cause for "unexplained" fetal death. Obstet Gynecol 1982. Nov;60(5):649-651 [PubMed] [Google Scholar]
11. Lionnet C, Body G, Gold F, Paillet C, Vaillant MC, Alle C, et al. Fetal cerebral accident due to massive fetomaternal hemorrhage. A case report. J Gynecol Obstet Biol Reprod (Paris) 1995;24(5):553-556 [PubMed] [Google Scholar]
12. Lau MS, Tan JV, Tan TY, Gomez JM, Yeo GS. Idiopathic chronic fetomaternal haemorrhage resulting in hydrops–a case report. Ann Acad Med Singapore 2003. Sep;32(5):642-644 [PubMed] [Google Scholar]
13. Evaluating fetomaternal hemorrhage by alphafetoprotein and Kleihauer following therapeutic abortions . D.L. Hay, [a], I. Horacek[a] and J. Paull[b] Department of Pathology, The Royal Women's Hospital, Melbourne, Australia Department of Anaesthetics, The Royal Women's Hospital, Melbourne, Australia. Received 18 May 1981; accepted 13 July 1981. Available online 10 April 2004.