Chronic Massive Fetomaternal Hemorrhage:
A Case Report

Yi-Giien Tsai, Chih-Hsing Hung, Shin-Nan Cheng, Yi-Ming Hua and Yeong-Seng Yuh

Fetomaternal hemorrhage (FMH) of more than 30 ml is relatively rare. In a complicated pregnancy, FMH of more than 30 ml occurs with the frequency of about 1/300. Massive FMH can cause severe neonatal anemia and even fetal death. We report a case of a male newborn, who was delivered at our hospital without perinatal asphyxia or obstetric complications. The baby was hemodynamically stable after birth, manifesting only pallor. The complete blood count revealed severe hypochromic anemia (hemoglobin 6.2 g/dL, hematocrit 20.5%) and reticulocytosis (reticulocyte 37.5%). There was no ABO blood type incompatibility and the result of direct Coomb’s test was negative. A Kleihauer-Betke stain on a maternal blood sample was performed and the result was positive with 16% red blood cells resistant to alkali, which is equivalent to 800 ml of fetal blood loss in the maternal circulation. After a packed red blood cell transfusion, the baby’s condition improved. (Clinical Neonatology 1998;5(1): 35-37)

Key word: Fetomaternal hemorrhage, Neonatal anemia, Kleihauer-Betke stain

The ability of fetal red cells passing the placental membrane was demonstrated by Chown in 1954 [1]. Fetal red cells in the maternal circulation can be detected with the Kleihauer-acid-elution method by relative acid resistance from fetal hemoglobin to adult hemoglobin [2]. About 40-50% of pregnancies usually in late gestation have fetal red cells in the maternal circulation [3]. In 98% of the cases, the loss of blood is minimal, usually only less than 0.1 ml [4]. Fetomaternal hemorrhage (FMH) of a significant volume (>30 ml) is rare with a frequency of about 1/300 [5]. Massive fetomaternal hemorrhage has been defined as bleeding in which more than 150 ml of fetal blood is found in maternal circulation [6]. Diagnosis is difficult and is usually made postpartum.

Case Presentation

A male neonate weighing 2,980 g was born by normal spontaneous delivery to a 34-year-old gravida III para II mother at 39 weeks of gestation. The mother had received amniocentesis at 18 weeks gestation. Ultrasound evaluation showed two sacs at 11 weeks gestation, however one sac disappeared at 14 weeks gestation. The biophysical profile was two weeks younger than expected gestation. The fetal heart rate (FHR) was normal and no obstetric complications were found. After birth, the Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. The baby had tachypnea, pallor, and edema gradually during the next 24 hours. A complete blood counts revealed that hemoglobin was 6.2 g/dl, hematocrit 20.5%, white blood cell count (corrected): 27.6 x 10^3/mm^3, white blood cell classification: neutrophils segment: 79%, lymphocytes: 15%, monocytes: 2%, eosinophils: 1%, basophils: 1%, atypical lymphocytes: 1%, meta-myelocytes: 1%, platelet count: 186 x 10^3/mm^3, reticulocytes 37.5%, nucleated red blood cells: 40/100 white blood cells. Red blood cells were hypochromic, macrocytic, and anisocytotic. The baby’s blood group (type O, Rh+) was the same as the mother’s. Both the direct Coombs’ test of the baby and the indirect Coombs’ test of the mother were negative. No hepatosplenomegaly or cephalohematoma was found. Sonography of the brain showed intraventricular hemorrhage with an echogenic area in the bilateral germinal matrix, about grade I to II. The maternal peripheral blood smear with Kleihauer-Betke stain (see Fig.1) showed 16% fetal cells which represented 800 ml of fetal blood loss in the maternal circulation on the basis of the 65 kg of the mother’s weight. Blood transfusion with 95 ml packed red blood cells was given and the baby’s condition improved. After transfusion, hemoglobin increased to 19.2 g/dl and hematocrit to 57.4%. Physical and neurological evaluations were normal when the infant was discharged on the sixth day of life.
Neonatal anemia can be induced by fetal hemorrhage (internal, external or intraplacental), fetal hemolysis or failure of RBC production. Anemia may be compensated at birth, or be only minimal if FMH has been less than 50 ml [5]. De Almeida and Bowman [7] defined massive FMH as more than 80 ml fetal blood loss occurred since neonatal anemia appeared at this level. Perinatal mortality due to massive FMH occurs in about 1 in 1,000 deliveries [8].

Most of the case reports have not explained the causes of the massive FMH. The risk factors of FMH include antepartum fetal death, cesarean delivery, abruptio placenta, placenta previa, manual removal of the placenta, intrapartum manipulation, antepartum genital bleeding, third-trimester trauma, and third-trimester aminocentesis [5]. Bowman and Pollock concluded that the risk of FMH of 20 ml or more in third-trimester aminocentesis was about 0.7% [9]. In our case, the obstetrician who performed the aminocentesis procedure denied traumatic tapping to placenta since the placenta was carefully localized by ultrasound monitoring.

Manifestation of FMH depends on the magnitude and the acuity of blood loss. Sinusoidal heart rate pattern and decrease in fetal movement are considered important signs of FMH [10]. Prenatal ultrasound studies could sometimes identify the presence of anasarca [11] or fetal growth retardation with a low biophysical score [12]. The non-stress test and ultrasound was useless for early diagnosis of FMH except in unusual cases [13]. The fetal heart rate of the baby in our study was normal and an ultrasound revealed that the baby was estimated to be younger than expected gestation which might be an evidence for early onset of fetomaternal hemorrhage in the pregnancy and resulted in chronic anemia.

Diagnosis of FMH can be confirmed by fetal RBC cells in the maternal blood with Kleihauer-Betke stain [2]. Elevated serum alph-fetoprotein may also be a sensitive indicator of FMH. A high level of alph-fetoprotein is associated with a number of pregnancy complications including intrauterine growth retardation, preterm delivery, late vaginal bleeding, pre-eclampsia, abruptio placenta, fetal death, placenta sonolucencies and fetal malformations, especially neural tube defects [12]. In combination with alph-fetoprotein, Kleihauer-Betke stain can provide a reliable diagnosis regarding FMH.

The red cell morphologic study of this infant indicated hypochromic anemia with an elevated normoblast count. The reticulocyte count was 37.5 %. Compared with the value of 3-7 % in normal newborn, this was markedly elevated [14]. This finding suggested that the course of blood loss was a chronic process, because that two to three days was usually required for a reticulocyte response to be observed, with a peak response after 10 to 14 days [15]. The estimated volume of fetal blood in maternal circulation was approximately 800 ml, which represented a loss of triple amount of the infant’s entire blood volume. Although a great amount blood was lost, the patient only demonstrated pallor with mild edema which indicated a chronic FMH with good compensation.

Neonatal deaths due to FMH are associated with shock at birth or soon after. Massive FMH that occurs on a more chronic basis and that allows fetal hemodynamic compensation usually has a good prognosis. As for massive FMH, the rapidity of the hemorrhage is probably a more important prognostic factor than the amount of fetal blood loss to the maternal circulation. Treatment of the anemic newborn following FMH depends primarily on the presence or absence of signs of circulatory failure. For those cases with chronic massive FMH, partial exchange transfusion is a better option [16]. In our case, in spite of the massive blood loss, the baby was born without shock and with normal Apgar scores. Because the baby gradually developed edema and tachypnea, he was treated with packed red blood cells transfusion and the condition improved.

FMH accounts for a significant portion of unexplained fetal deaths [12]. When there is an anemic newborn without clues of hemolytic disease, obstetric hemorrhage, decreased RBC production, or neonatal hemorrhage, the Kleihauer-Betke stain with alpha-fetoprotein analysis should be performed for consideration of FMH.

**Fig. 1.** Kleihauer-Betke acid-elution preparation of maternal postpartum peripheral blood. The fetal red cells derived from leakage of the infant’s blood into the maternal circulation are rich in hemoglobin F and are stained darkly.
References