Persistent reversed end diastolic flow in the fetal middle cerebral artery: an ominous finding

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Abstract

Fetal persistent middle cerebral artery reversed end diastolic flow is a rare and ominous finding. Previous cases have been associated with intracranial hemorrhage, growth restriction, anaemia, and hepatic anomaly. Intrauterine demise or early neonatal death is a common outcome. We report the case of persistent middle cerebral artery reversed end diastolic flow in a well-grown fetus at 32 weeks' gestation resulting from acute, severe anaemia due to a large feto-maternal hemorrhage. An emergency cesarean section was performed and the neonate required advanced resuscitation and immediate blood transfusion. Postnatal magnetic resonance imaging confirmed a hemorrhagic parietal infarct and bilateral ischaemic changes in the basal ganglia. This provides further evidence that persistent middle cerebral artery reversed end diastolic flow in any fetus is an ominous finding warranting urgent diagnostic evaluation and/or delivery.

Keywords: Reversed end diastolic flow, anaemia

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Introduction

Middle cerebral artery Doppler examination is increasingly being performed as a measure of fetal well-being at ultrasound. Reversed end diastolic flow in the middle cerebral artery (MCA-REDF) is thought to occur due to increased intra-cerebral pressures. This is most commonly caused by excessive transducer probe pressure, which leads to transient reversal of flow that quickly resolves after readjustment of the probe.¹ Persistent MCA-REDF is rare and there have only been six reported cases in the literature.^{1–6} These cases have been associated with fetal growth restriction, anaemia, intraventricular hemorrhage, and a rare hepatic anomaly, which likely cause increased intra-cerebral pressure and result in the ultrasound finding of persistent MCA-REDF. All documented cases have resulted in devastating outcomes of fetal or neonatal death and disability. This highlights the importance of early recognition of persistent MCA-REDF and urgent assessment or delivery of the fetus.

We report the rare case of a healthy multigravida at 32 weeks' gestation presenting for a routine growth scan with a finding of persistent MCA-REDF in a well-grown fetus due to a large feto-maternal hemorrhage. We reviewed the literature and outcomes of cases of persistent MCA-REDF.

Case report

A healthy 36-year-old multigravida with a well-dated and uncomplicated singleton pregnancy presented for evaluation of fetal growth at 32 weeks' gestation as her previous pregnancy was complicated by preeclampsia and fetal growth restriction. The estimated fetal weight was appropriate for 32 weeks' gestation (1930 g; 30th customized centile⁷), the amniotic fluid index was 12 cm, and the umbilical artery pulsatility index was normal at 1.07. The MCA peak systolic velocity was elevated at 95 cm/s (2.13 Multiples of Median; normal range 37.2–68.2 cm/s for this gestation), consistent with severe fetal anaemia, and there was persistent MCA-REDF (Figure 1). There was mild fetal ascites, but a positive a-wave in the ductus venosus with normal pulsatility index for veins (0.74). No fetal breathing or body movements were noted and 30-min cardiotocography was non-reassuring with no accelerations and absent variability (Figure 2), giving a biophysical score of 2/10. An emergency cesarean section was performed for presumed severe fetal anemia, and a male infant was delivered in poor condition with birth weight 2040 g, and Apgar scores of 2 at 1 min and 3 at 5 min. The cord haemoglobin was 9 g/L (normal range 120–180 g/L). There was a good response to intubation and transfusion was initiated immediately. Arterial cord gases showed a pH of 7.16, lactate of 8.5, and a base excess of –11 indicative of hypoxia.

Figure 1 Reversed diastolic flow in the middle cerebral artery

Figure 2 Cardiotocograph trace immediately following the ultrasound demonstrating (a) fetal heart rate, (b) maternal heart rate and (c) uterine activity

Investigations for anemia confirmed a large fetomaternal hemorrhage with a positive maternal Kleihauer test, and flow cytometry confirming 2.3% cells of fetal origin in the maternal circulation, correlating to 57 mL of fetal whole blood. No maternal red blood cell antibodies were present, fetal and maternal platelet counts were normal and parvovirus screen was negative. Placental histopathology

showed increased nucleated fetal erythrocytes consistent with anaemia.

The baby required respiratory support for the first 11 days, and phenobarbitone was necessary for seizure control. Cranial ultrasound performed on day 5 confirmed a hemorrhagic infarct in the right parietal area, and magnetic resonance imaging subsequently confirmed these findings

Table 1 Summary of published cases of persistent reversed diastolic flow in the middle cerebral artery and outcome

Paper	Management	Outcome	Cause
Hirshberg et al. ²	27 + 5 weeks' gestation Managed expectantly	Fetal death in utero	Intraventricular hemorrhage
Kawakita et al. ³	27 + 3 weeks' gestation Managed by cesarean section	No neonatal follow up recorded	Severe growth restriction
Giancotti et al. ⁴	27 weeks' gestation Managed expectantly	Neonatal death	Intrahepatic bile duct malformation
Baschat et al. ⁵	29 + 2 weeks' gestation Managed by cesarean section	Grade III intraventricular hemorrhage Periventricular leukomalacia Moderate respiratory distress syndrome	Feto-maternal hemorrhage
Respondek et al. ¹	31 weeks' gestation Managed expectantly	Fetal death in utero	Rhesus disease
Sepulveda et al. ⁶	30 weeks' gestation Managed expectantly	Fetal death in utero	Severe growth restriction

as well as bilateral ischaemic and hemorrhagic changes in the basal ganglia. The baby was discharged home on Day 37 with a plan for ongoing paediatric neurodevelopmental follow-up.

Discussion

MCA assessment is performed to assess fetal well-being at ultrasound. In the hypoxic fetus, the cerebral vasculature dilates and this causes a reduction in the MCA pulsatility index in a phenomenon known as "brain sparing".^{8,9} With disease progression the fetus is no longer able to compensate, and resistance in the MCA increases.^{8,10} In the preterm (<32 weeks) small for gestational age fetus, MCA Doppler has limited accuracy in predicting acidemia in the absence of other Doppler abnormalities. In the term small for gestational age fetus with normal umbilical artery Doppler, an abnormal MCA Doppler (PI < 5th centile) has moderate predictive value for acidosis at birth and should be used to time delivery.¹¹

Transient MCA-REDF likely occurs due to excessive external probe pressure and is an artifact that is of no clinical consequence.¹ When this occurs, it is suggested that the measurements are repeated and confirmed by a second operator with attention to minimizing transducer pressure. Rarely, persistent MCA-REDF occurs and there are currently only six reported cases in the literature (Table 1).¹⁻⁶ These cases were caused by excessive intracranial pressure resulting from intracranial hemorrhage,² severe anaemia^{1,5} or severe fetal growth restriction,^{3,6} and a rare intrahepatic bile duct malformation.⁴ All reported cases have had devastating outcomes with fetal or neonatal death occurring in four of the six cases (Table 1).^{1,2,4,6} One of the survivors suffered a grade III intraventricular hemorrhage and periventricular leukomalacia.⁵ Neonatal outcomes were not recorded for the other survivor.³

In our case, feto-maternal hemorrhage caused severe fetal anaemia that likely precipitated a cerebral hemorrhagic infarct and edema. This likely led to raised intracranial pressure and resulted in the ultrasound finding of persistent MCA-REDF. There has been one previous case of MCA-

REDF in association with feto-maternal hemorrhage⁵ and a similar observation in a case of severe rhesus disease.¹ Severe fetal anaemia should be considered as a potentially treatable cause of MCA-REDF. The long-term outlook will be determined by whether irreversible damage has already occurred, and follow-up antenatal or postnatal neuroimaging is recommended in survivors.

While MCA-REDF is most commonly seen as a result of increased transducer pressure, our study and review of the literature provide further evidence that persistent MCA-REDF is an ominous sign, associated with high perinatal morbidity and mortality. It is essential that ultrasonographers are aware of the diagnosis and implications of fetal MCA-REDF and it is reported in future studies on MCA-PI. This case highlights the importance of urgent further investigations to evaluate fetal well-being or prompt delivery if persistent MCA-REDF is seen and that severe fetal anaemia is a potentially treatable cause.

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Ethical approval: This study was approved by the Mercy Hospital for Women Human Research Ethics Committee and written consent was obtained from the patient for publication of the details and images from this case.

Guarantor: FCB

Contributorship: FCB and CAC managed the patient and researched the literature. FCB, CAC, and SPW designed the review and the report. FCB wrote the initial version of the manuscript and CAC and SPW edited the manuscript. All authors reviewed and approved the final version of the manuscript.

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