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A Rare Case: Persistent Reverse End Diastolic Flow (PREDF) in Fetal Middle Cerebral Artery During Mid Trimester in Pregnant Patient with Cardiac disease, Preceding Poor Fetal Outcome

Abstract:

Background- Persistent reverse end-diastolic flow (PREDF) in the fetal middle cerebral artery (MCA) is a rare but critical Doppler finding indicating severe fetal compromise. Normally, fetal cerebral circulation shows high resistance; during hypoxemia, impedance decreases to maintain cerebral perfusion through the brain-sparing effect. PREDF represents failure of this autoregulatory mechanism and reflects advanced hemodynamic deterioration. It is associated with conditions such as fetal growth restriction, fetalanemia, hydrops fetalis, intracranial hemorrhage, and hepatic abnormalities.

Materials and Methods- A 22-year-old pregnant woman with underlying cardiac disease was evaluated at 23 weeks and 3 days of gestation (as per LMP) using serial fetal Doppler ultrasonography.

Results- Doppler examination demonstrated PREDF in the MCA along with early fetal growth restriction, hydrops fetalis (ascites, pleural effusion, and subcutaneous edema), severe ventriculomegaly, cerebellar hypoplasia, porencephalic cystic changes, and significant oligohydramnios. Progressive fetal compromise was noted on follow-up scans.

Conclusion- PREDF in the fetal MCA is an ominous late marker of fetal distress. Despite monitoring, the pregnancy resulted in intrauterine fetal demise, and a dead fetus was delivered vaginally at 29 weeks and 5 days of gestation. This case highlights the grave prognostic implication of PREDF, especially in high-risk pregnancies.

Keywords: persistent reversed end diastolic flow; middle cerebral artery; hydrops fetalis; last menstrual period

1. Introduction

Middle cerebral arteries (MCAs) are the most accessible cerebral vessels for Doppler assessment and contribute to nearly 80% of total cerebral blood flow[1]. They arise as major branches of Circle of Willis from internal carotid arteries. Under normal conditions, fetal cerebral circulation is characterized by high vascular resistance. In pediatric and adult populations, persistent reverse end-diastolic flow (PREDF) in the middle cerebral artery reflects cessation of effective cerebral circulation and is therefore used as an ancillary test to support the diagnosis of brain death or death by neurological criteria. However, the significance of this Doppler finding differs fundamentally in the fetus. Unlike in adults, fetal cerebral circulation is physiologically dynamic and influenced by placental oxygenation and compensatory autoregulatory mechanisms. In the fetus, PREDF represents severe hypoxia,

rising intracranial pressure, and failure of cerebral autoregulation rather than irreversible cessation of brain function. Because fetal cardiac activity and placental circulation may still be present, this finding does not equate to brain death in utero but instead indicates critically advanced fetal compromise with a very high risk of impending intrauterine demise. In hypoxemia, this resistance decreases, allowing redistribution of blood to vital organs, particularly the brain—an adaptive mechanism known as brain-sparing effect[2]. This change is an early Doppler marker of fetal autoregulation. PREDF may occur due to elevated intracranial or extracranial pressure, cerebral edema, or profound hypoxemia[1,2].

2. Case Presentation

Patient G1P0A0, aged 22 years, with gestational age of 23 weeks and 3 days according to last menstrual period (LMP) presented with complaint of pain in lower abdomen after cardiac surgery (aortic valve replacement). Then we have performed fetal ultrasound scan with color doppler at multiple visits of patient and fetal ultrasound scan showed features like early fetal growth restriction, changes of hydrops fetalis (ascites, pleural effusion andsubcutaneous edema), changes of fetal hypoxia like porencephalic cysts/cystic encephalomalacia with cystic degeneration/central cystic encephalomalacia of bilateral cerebellar hemispheres, cerebellar hypoplasia, severe ventriculomegaly and significant oligohydramnios.

On her first visit at 23 weeks and 3 days as per her LMP, the ultrasound examination showed a breech lie fetus with mildly reduced amniotic fluid. Other ultrasound findings include mild bilateral pleural effusion within the fetal thorax with mild fetal ascites, fetal pericardial effusion and subcutaneous edema**(Figure A)**. On spectral doppler, reversal of end diastolic flow was noted in bilateral fetal middle cerebral artery **(Figure B)**.

On her visit at 29 weeks and 2 days as per her LMP, reversal of end diastolic flow in bilateral fetal middle cerebral artery and other findings of previous visit persisted along with reduced fetal weight (<3rd centile), suggestive of early FGR. Fetal brain developed periventricular echogenicity along with increased echogenicity of bilateral thalami and features of fetal brain degeneration like porencephalic cyst/cystic encephalomalacia, central cystic degeneration of bilateral cerebellar hemispheres along with mild cerebellar and vermian hypoplasia and shallow sylvian fissures **(Figure C)**. Bilateral lateral ventriculomegaly became severe along with dangling of choroid plexuses (Right lateral ventricle diameter - 16.4 mm, and left lateral ventricle diameter - 16.5 mm) with mildly dilated 3rd (diameter - 3.3 mm) and 4th (diameter - 5.1mm) ventricles, suggestive of quadriventriculomegaly**(Figure D)** along with further brain degeneration.

A dead fetus was born with vaginal delivery at 29 weeks and 5 days of gestation (as per her LMP) and 26 weeks and 5 days of gestation (as per her ultrasound scan) weighing 1.195 kg. The mother's condition after delivery was stable. The mother was discharged from the hospital in good condition after her post-operative care.

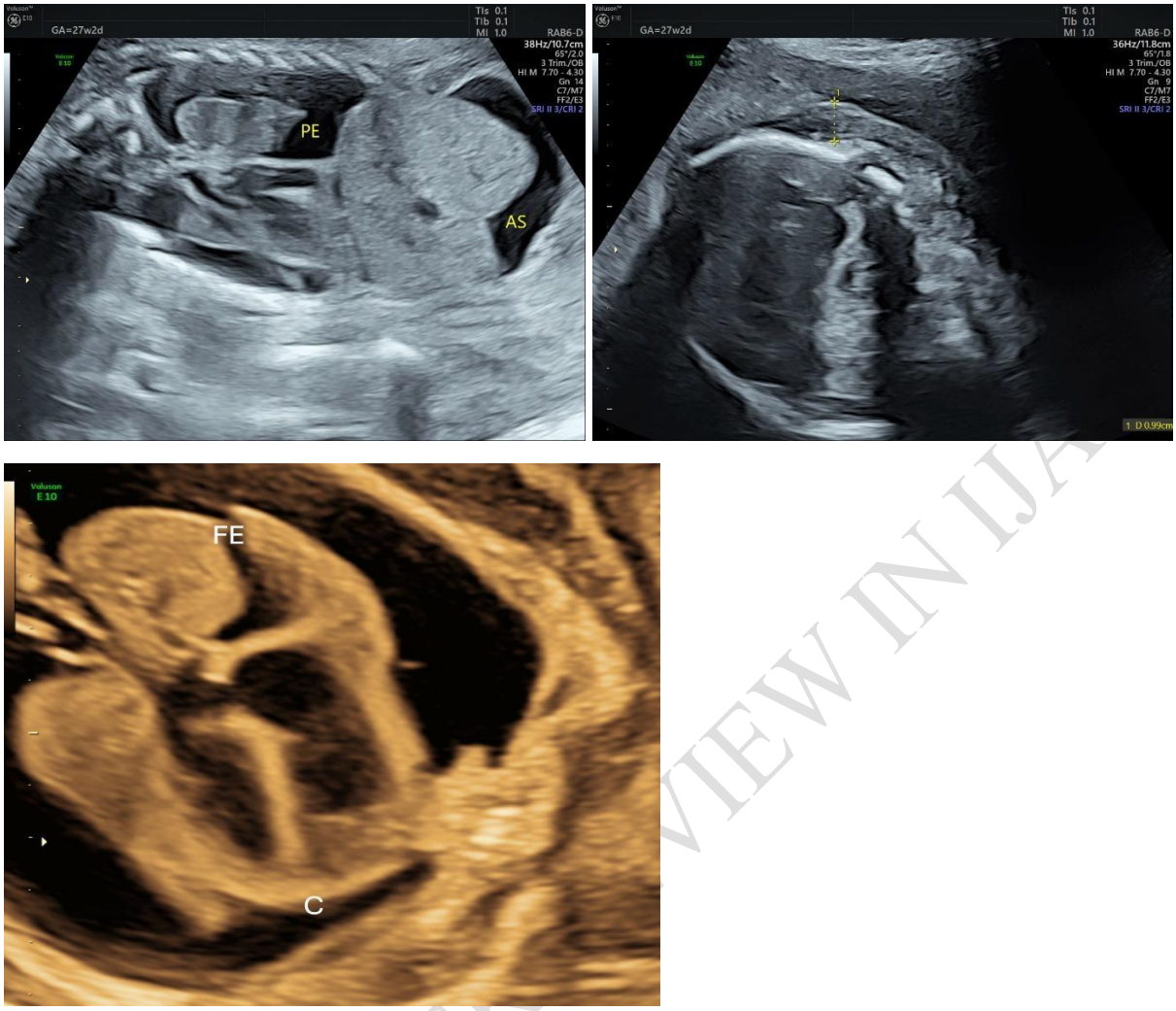


Figure A. Changes of hydrops fetalis like fetal ascites, pleural and pericardial effusion and subcutaneous edema. (PE = Pleural effusion; AS = ascitic fluid; 1 = Subcutaneous edema; C = Pericardial effusion; FE = Extension of pleural fluid into pleura fissures in pleural effusion)

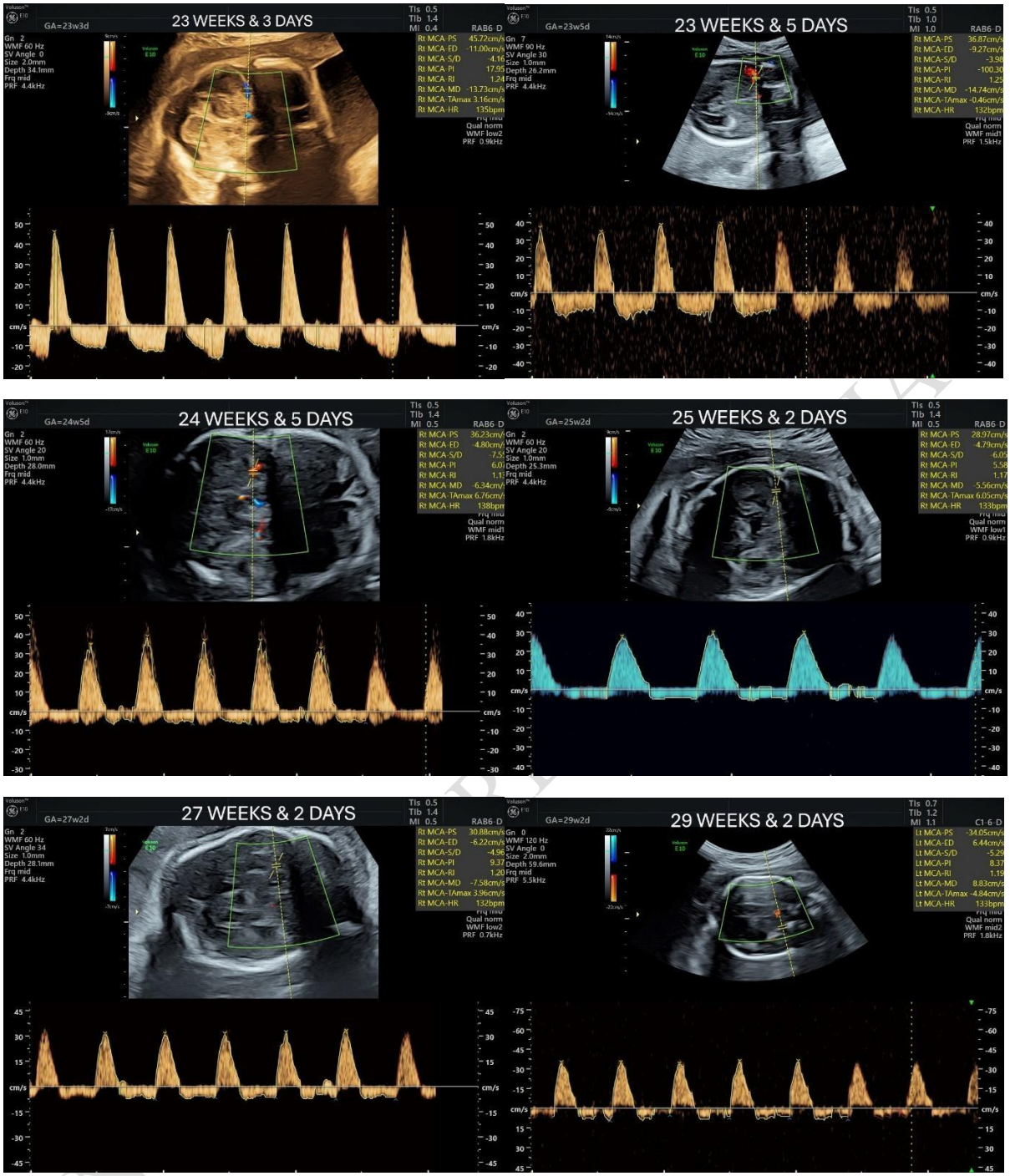
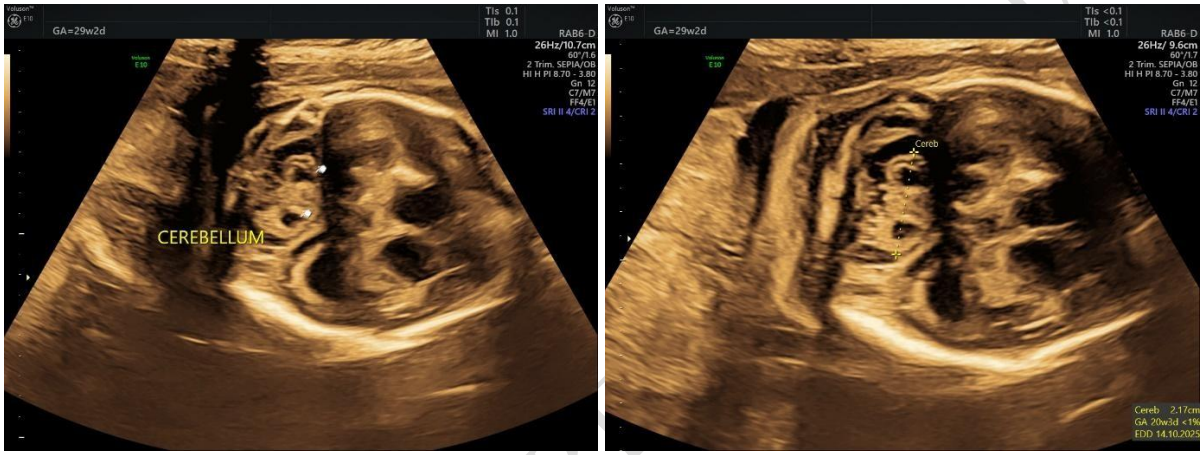


Figure B. PREDF in bilateral fetalMCA on multiple visits (from first visit to last) as shown in images.



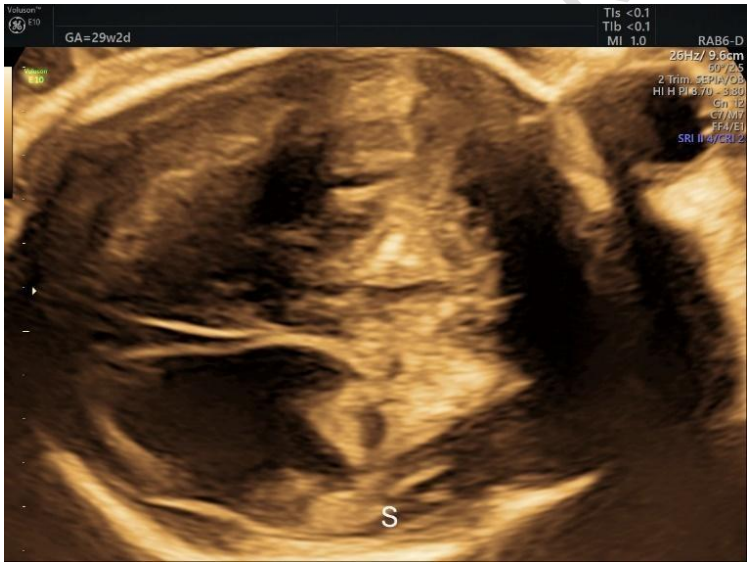


Figure C. Hypoechoic area adjacent to occipital horn of left lateral ventricle: cystic cerebral degeneration with encephalomalacia (#) with cystic encephalomalacia andcerebellar hypoplasia (<1 centile) along with bilateral shallow sylvian fissures. (S = Sylvian fissure; Cereb = Cerebellum)

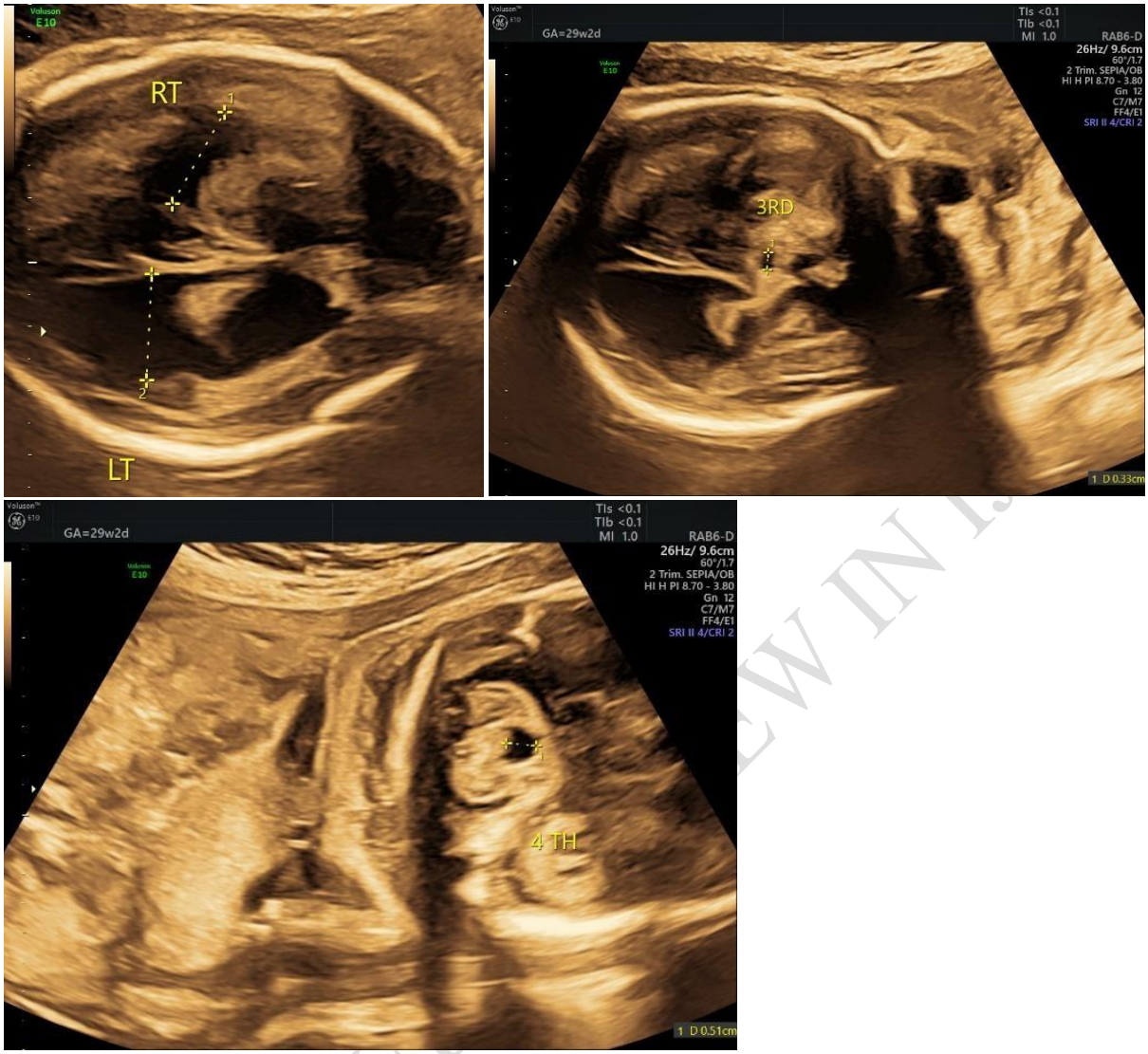


Figure D. Bilateral lateral ventriculomegaly (Right - 16.4 mm; left - 16.5 mm) with mildly dilated 3rd (3.3 mm) and 4th (5.1mm) ventricles: Quadriventriculomegaly. (RT = Right lateral ventricle; LT = Left lateral ventricle; 3RD = 3rd ventricle; 4TH = 4th ventricle)

3. Discussion

Doppler ultrasound is widely used to assess fetal circulation, with middle cerebral artery (MCA) evaluation crucial for detecting hypoxia and growth restriction. Normally high-resistance, bilateral MCA shows reduced pulsatility index (PI) in hypoxemia due to brain-sparing. In severe or prolonged hypoxia, cerebral edema and raised intracranial pressure may cause reversed end-diastolic flow (REDF), a rare and ominous marker of terminal compromise. Persistent REDF (PREDF) is strongly associated with poor outcomes, including intrauterine death, especially in cases of fetal growth restriction and hydrops fetalis, consistent with previous studies[3,4].Persistent reverse end-diastolic flow (PREDF) in bilateralfetal MCA is an exceptionally rare but ominous Doppler finding that reflects severe hemodynamic compromise and is strongly associated with poor perinatal outcomes. A review of published case reports highlights diverse aetiologies, management strategies, and uniformly adverse prognoses.

Brownfoot et al. reported PREDF at 32 weeks' gestation in the setting of severe fetomaternal haemorrhage, where emergency caesarean delivery was performed, but the neonate subsequently developed a haemorrhagic parietal infarct with ischemic basal ganglia changes, indicating profound antenatal hypoxic–ischemic brain injury despite timely intervention[5]. Similarly, Baschat described a case at 29+2 weeks where caesarean section was performed, but the newborn suffered intraventricular haemorrhage, periventricular leukomalacia, and respiratory distress syndrome[2]. Other reports underscore poor outcomes with expectant management: Sepulveda et al. noted fetal demise in early-onset growth restriction[4], while Respondek et al. documented intrauterine death at 31 weeks due to Rhesus disease[6].

Neonatal mortality was a recurrent outcome in reported cases of PREDF. Setiawan et al. documented a case at 30 weeks of gestation complicated by severe early-onset fetal growth restriction, where emergency caesarean section was performed due to worsening Doppler findings. Despite timely intervention, the neonate succumbed shortly after birth, underscoring the grave prognosis associated with PREDF even when delivery is expedited[7]. Similarly, Giancotti et al. described a fetus at 27 weeks with PREDF in the middle cerebral artery associated with a rare congenital intrahepatic bile duct malformation. In this instance, although delivery was attempted, the neonate did not survive, reflecting the combined impact of structural anomalies and advanced hemodynamic deterioration[8].

Table 1. Case Reports on PREDF in the MCA and Associated Outcomes

No.	Article	Gestation	Management	Cause	Outcome
1	Baschat et al.[2]	29+2 weeks	Cesarean section	Feto-maternal hemorrhage	Intraventricular hemorrhage, periventricular leukomalacia, moderate respiratory distress syndrome
2	Kawakita et al.[3]	27+3 weeks	Cesarean section	Severe fetal growth restriction	No neonatal follow-up recorded
3	Sepulveda et al.[4]	30 weeks	Expectant	Severe fetal growth restriction	Intrauterine fetal death

4	Browfoot et al.[5]	32 weeks	Cesarean section	Feto-maternal hemorrhage	Hemorrhagic parietal infarct and bilateral ischemic changes in basal ganglia
5	Respondek et al.[6]	31 weeks	Expectant	Rhesus disease	Intrauterine fetal death
6	Setiwan et al.[7]	30 weeks	Cesarean section	Severe fetal growth restriction	Neonatal death
7	Giancotti et al.[8]	27 weeks	Expectant	Intrahepatic bile duct malformation	Neonatal death
8	Our case	Multiple visits from 23+3 weeks to 29+5 weeks	Expectant medical management and vaginal delivery	Early fetal growth restriction, hydrops fetalis (ascites, pleural effusion and subcutaneous edema), changes of fetal hypoxia like porencephalic cysts /cystic encephalomalacia with cystic degeneration /central cystic encephalomalacia of bilateral cerebellar hemispheres, cerebellar hypoplasia, severe ventriculomegaly and significant oligohydramnios	Intrauterine fetal death

4. Conclusion

Our present case aligns with this pattern, with PREDF detected from 23 weeks in a patient with cardiac disease, early fetal growth restriction, hydrops, cerebral cystic changes, cerebellar hypoplasia, ventriculomegaly, and oligohydramnios. Despite monitoring, intrauterine fetal death occurred at 29+5 weeks.PREDF in bilateral fetalmiddle cerebral artery, observed in a mid-trimester pregnancy with cardiac disease and severe fetal complications, indicated advanced fetal compromise and culminated in intrauterine demise, underscoring its critical prognostic significance for timely management.

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