

Congenital CMV infection associated with abnormal MCA PSV

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Abstract

Middle Cerebral Artery peak systolic velocity (MCA PSV) measurement remains the gold-standard screen for intrauterine fetal anaemia. Readings above 1.5 multiple of median suggest moderate to severe anaemia and warranting further investigation.

Primary cytomegalovirus (CMV) infection in pregnancy is the leading cause of sensorineural deafness in the new-born, and is also associated with neurodevelopmental delay and more severe neurological sequelae.

We report a case of elevated MCA-PSV Dopplers in a fetus undergoing antenatal surveillance for anaemia who, following delivery was found to a normal haemoglobin and thrombocytopaenia due to congenital CMV infection.

Introduction

Fetal anaemia is a rare but serious condition that can have significant consequences. It can be classified into immune or non-immune causes.

The most common immune-mediated cause is red cell haemolysis due to alloimmunisation. Non-immune causes include infection, erythropoiesis disorders, fetal or placental vascular tumors, fetomaternal hemorrhage, vasa praevia, and complications of monochorionicity in multifetal pregnancies.

Certain red cell antibodies, such as D, c, c+E, and K (K1), frequently lead to severe fetal and neonatal anaemia, while others like E, C, e, Ce, k(K2), Fya, Fyb, S, s, U, M, and Jka are encountered less frequently but can still cause severe neonatal anaemia.

Doppler ultrasound measurement of MCA-PSV is a reliable and non-invasive screening method for fetal anaemia. It has a sensitivity of 100% for moderate to severe anaemia, with a false positive rate of 12%. A cut-off MCA-PSV of >1.5 multiples of the median (MoM) is used to recommend further interventions such as cordocentesis and possible intrauterine blood transfusion (IUT).

Case report

A 36-year-old healthy parous woman, with a previously healthy uncomplicated pregnancy was referred for fetal medicine review following the detection of Anti-M antibodies. Anti-M is considered a rare cause of fetal anaemia and she was evaluated at 24 and 34 weeks for fetal anaemia. Her blood group was B Rh (D) positive. She had a normal routine dating and anomaly scans performed at 12 and 20 weeks of gestation. An ultrasound was performed also at 25 weeks to screen for fetal anaemia and the MCA-PSV was normal.

At 34 weeks the MCA-PSV was markedly elevated (maximum velocity 103.7 cm/s), >1.55 MoM. The fetal growth, liquor volume and umbilical artery Dopplers (UAD) were all within the normal range. However, there was no evidence of fetal hydrops and tricuspid regurgitation was not apparent, and the fetus was active.

The differential diagnosis included rhesus isoimmunisation, Parvovirus B19 infection or acute fetomaternal haemorrhage (FMH). A TORCH screen, Parvovirus serology and Kleihauer-Betke tests were performed. A cardiotocograph (CTG) was performed and this was reassuring. The Kleihauer test was negative and Parvovirus antibodies were absent. The woman was admitted to hospital for observation and antenatal corticosteroids were administered.

The MCA PSV Dopplers remained elevated on the following day and unprovoked decelerations were observed on routine CTG monitoring. A decision was taken to deliver the baby due to non-reassuring CTG monitoring in the background of possible fetal anaemia. An emergency caesarean section (CS) was performed.

A healthy baby was delivered by CS, weighing 2.2Kg with normal Apgar and cord gases. A cord blood sample was also sent immediately for FBC. At CS, the amniotic fluid was noted to be foul smelling, suggestive of a possible intrauterine infection. Fetal and placental swabs were taken.

The cord and neonatal Hb was normal however there was severe neonatal thrombocytopenia. The baby appeared jaundiced with a petechial rash and hepatosplenomegaly was noted. The infant was admitted to the neonatal intensive care unit (NICU) and received a platelet transfusion and phototherapy.

Four days following the delivery, microbiological tests confirmed a recent maternal CMV infection. The Anti-CMV IgG avidity was high (0.759), a result that suggested that the primary infection had occurred within three months from the time of the testing. Microbiological testing also confirmed congenital CMV in the neonate.

Fig A: Demonstrating MCA

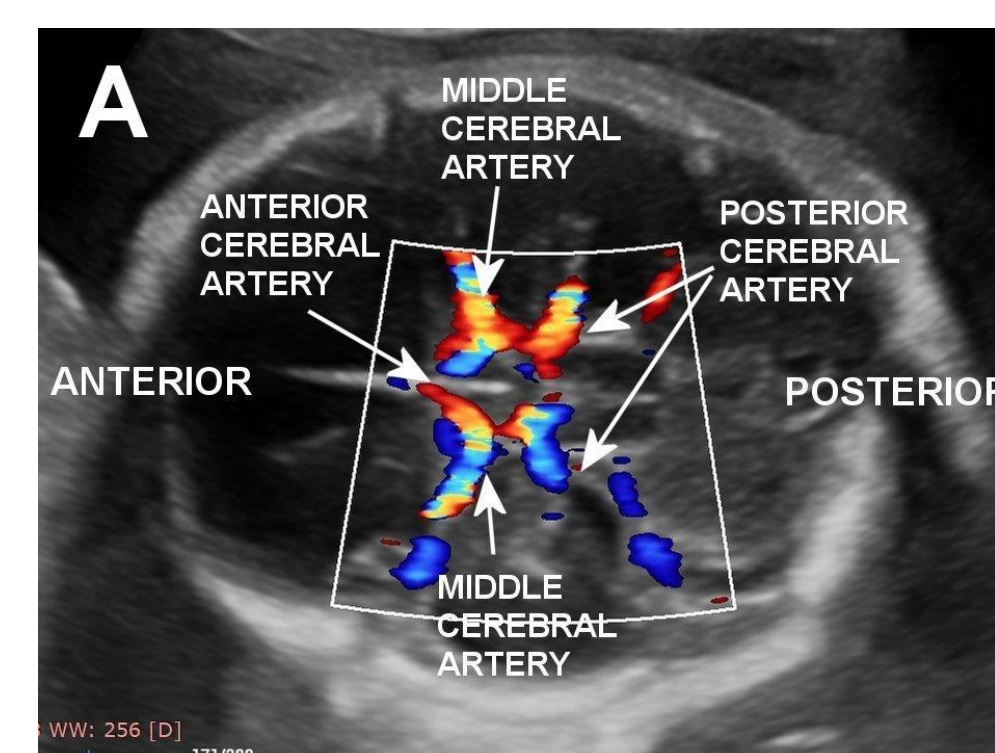
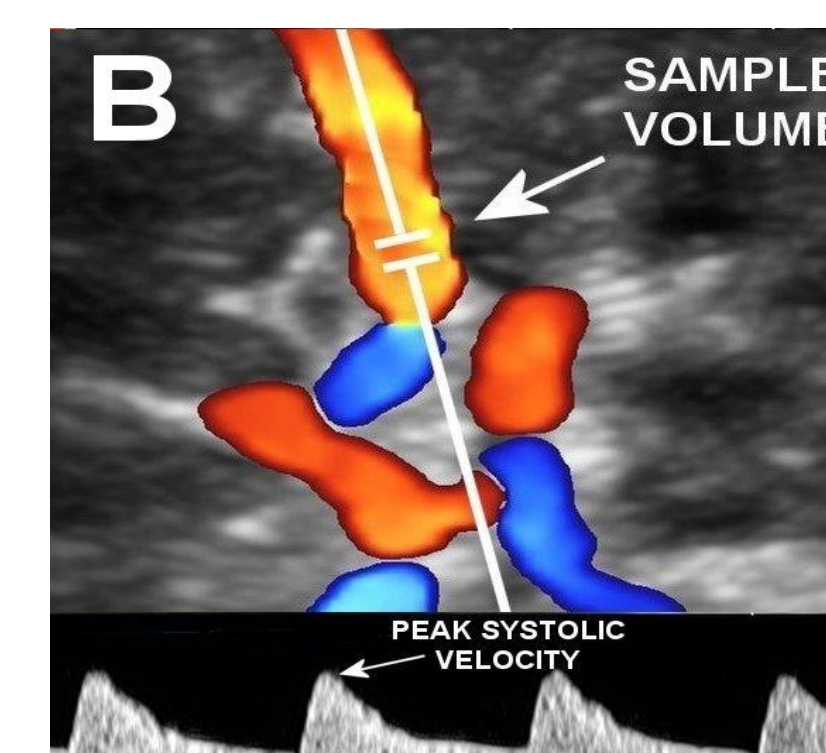


Fig B: Demonstrate the location and angle of measurement of MCA.



Discussion

CMV infections are mostly asymptomatic and self-limiting in healthy adults. The incidence of congenital CMV is estimated to be 0.5% and the risk of fetal transmission if the primary infection occurred in the first or second trimester is thought to be 30% to 40% increasing to 70% if the primary infection occurs within the third trimester. However, only 10 to 15% of neonates with congenital CMV will manifest clinical signs at birth.

There are multiple reported cases of immune thrombocytopenia (ITP) triggered by viral infections such as CMV. Severe and life-threatening haemorrhage secondary to ITP is very rare occurring in <1%. There are reported cases of extremely high MCA-PSV in cases of congenital CMV infection in both anaemic and non-anaemic neonates. Although there is no clear aetiology identified, there are multiple theories on to why the MCA-PSV may become elevated in these cases.

Increased MCA mean velocity following bacterial or viral central nervous system (CNS) infections has been previously demonstrated in adult patients and it is suggested that these features result from an inflammatory hyperaemia due to infection. CMV has also been shown increase arterial blood pressure in adult patients, which may alter the circulation within the cerebral vessels.

It is alternatively possible that the extremely raised MCA-PSV is secondary to reduced blood viscosity resulting from thrombocytopenia. A combination of these factors may be at play.

Given the high prevalence of CMV and congenital CMV infections, we would recommend screening for CMV infection in addition to Parvovirus B19 when encountering an unexpectedly high MCA-PSV, particularly in fetuses not at risk of anaemia. Similarly, we suggest examination of the MCA-PSV whenever a case of congenital CMV infection is suspected antenatally.

References

Castleman MRCOG JM, Gurney MRCOG L, Kilby DSc FRCOG FRCPi M, Katie Morris MRCOG R, Morris K. Identification and management of fetal anaemia: a practical guide. *Obstet Gynaecol.* 2021 Jul 1;23(3):196–205. The Management of Women with Red Cell Antibodies during Pregnancy Green-top Guideline No. 65. 2014; Mari G, Adrignolo A, Abuhamad AZ, Pirhonen J, Jones DC, Ludomirsky A, et al. Diagnosis of fetal anemia with Doppler ultrasound in the pregnancy complicated by maternal blood group immunization. *Ultrasound Obstet Gynecol.* 1995;5(6):400–5. Management of Alloimmunization During Pregnancy | ACOG. Heyborne K. Elevated Middle Cerebral Artery Peak Systolic Velocity in a Nonanemic Fetus with Alpha-Thalassemia Trait. *Obstet Gynecol.* 2009;2009:1–2. Babic I, Ferretti E, Jimenez-Rivera C, Gruslin A, Moretti F. Prenatal diagnosis of intrahepatic portosystemic shunt in intrauterine growth restricted fetus with transient fetal anemia and cardiomegaly: A case report. *J Case Reports Images Obstet Gynecol.* Boppana SB, Fowler KB, Britt WJ, Stagno S, Pass RF. Symptomatic congenital cytomegalovirus infection in infants born to mothers with preexisting immunity to cytomegalovirus. *Pediatrics.* 1999 Jul; 104(1 Pt 1):55–60. Jin MJ, Kim Y, Choi EM, Shim YJ, Kim HS, Suh JK, et al. Clinical characteristics and treatment courses for cytomegalovirus-associated thrombocytopenia in immunocompetent children after neonatal period. *Blood Res;*53(2):110. Butros LJ, Bussell JB. Intracranial hemorrhage in immune thrombocytopenic purpura: a retrospective analysis. *J Pediatr Hematol Oncol.* 2003 Aug; 25(8):660–4. Duncan JR, Schenone MH, Argoti PS, Mari G. Middle cerebral artery peak systolic velocity in perinatal cytomegalovirus infection. *J Clin Ultrasound.* 2019 Jul 1;47(6):372–5. Nagel MA, Traktinskiy I, Stenmark KR, Frid MG, Choe A, Gilden D. Varicella-zoster virus vasculopathy: immune characteristics of virus-infected arteries. *Neurology.* 2013 Jan 1;80(1):62–8. Cheng J, Ke Q, Jin Z, Wang H, Kocher O, Morgan JP, et al. Cytomegalovirus Infection Causes an Increase of Arterial Blood Pressure. *PLOS Pathog.* 2009 May [cited 2022 Jun 23];5(5):e1000427. Fig A and B Perinatology.