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Case Report

Radiology Section

Elevated Fetal Middle Cerebral Artery Peak Systolic Velocity: Anemia if Not; Then What?

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ABSTRACT

It is now a globally accepted and time tested fact that elevated fetal middle cerebral artery peak systolic velocity as seen on color Doppler is a non-invasive indicator of fetal anemia. Cases describing causes of raised fetal middle cerebral artery peak systolic velocities in the absence of moderate to severe fetal anemia are very rare.

We describe one such rare case of a nearly full term male of a diabetic mother whose middle cerebral artery peak systolic velocities were persistently raised in the absence of any fetal anemia; both in the intra as well as the early extra uterine state of its being. Hypertrophic cardiomyopathy in this neonate of a diabetic mother was found to be the cause of this temporary increase in blood velocity. The raised values eventually normalized by the 10th day of life by which time the cardiac status of the neonate had improved and stabilized following appropriate medications. Thus fetal anemia alone is not the exclusive cause of elevated fetal middle cerebral artery peak systolic velocities. Elevated velocities in absentia of fetal anemia should prompt an active search for other possible causes, one of which is as mentioned in this report.

Keywords: Cardiomyopathy, Colour doppler ultrasound, Diabetic mother, Fetus

CASE REPORT

A 26-years-old pregnant lady who was diagnosed to have non insulin dependent diabetes mellitus was referred for obstetric ultrasound in Rural Medical College, Loni, Maharashtra, India. She was a primi gravida and had no other significant illnesses in the past, especially pertaining to her cardiovascular system. Her blood sugar was under control on oral hypoglycemics alone before as well as during the pregnancy. She had been on oral hypoglycemisc for almost last two years.

Obstetric ultrasound was performed after informed written consent as per the existing law of this land. Ultrasound revealed a single intrauterine live gestation of average gestational age 35 weeks. This patient presented to us for the first time. She had no earlier obstetric ultrasound reports. As color doppler demonstrated an abnormally elevated fetal Middle Cerebral Artery Peak Systolic Velocity [Table/Fig-1] of 70 cm/s that was more than 1.5 times the MoM value for that particular GA [41 +/- 8 cm/s] by local as well as international standards [1-6]; a diagnosis of severe fetal anemia was suggested. Each wave was tall and belonged to KG Type III waveform as per the Kachewar Gandage classification system for types of fetal MCA velocity waveform patterns [7]. In addition, as the Amniotic Fluid Index [AFI] was 22 cm the diagnosis of polyhydramnios too was mentioned. A Grade III placenta with normal placental thickness (3.2 cm) was seen. Soft tissues of the fetal thoracic wall [Table/Fig-2] as well as the abdomen were thick. The fetal cardiac interventricular septum too was thickened [10 mm]. There was however no abnormal pleural, pericardial or peritoneal free fluid.

Due to the prenatal sonographic suggestion of severe fetal anemia and the presence of polyhydramnios in this known diabetic mother, lower segment caesarean section was immediately performed [Hence we could not obtain multiple measurements that are recommended to determine the trend of increasing values] and a 3999 grams male child was born. A pan systolic murmur and a bluish tinge to the child's overall appearance were noted. Pulse Oximeter demonstrated a saturation of only 76% without oxygen and that of 91% with 100% oxygen. The neonate was shifted to neonatal intensive care unit (NICU) for further management.

The fetal blood sugar level was 56gm/dl. On delivery the neonate had a hemoglobin value of 15.6 gm/dl. On day 2 and day 3 it was 15.2 and 16.4 gm/dl respectively. Total Bilirubin on day 1 was 1.9 and that on day 3 was 5.9. The mother was O Rh positive and the child`s blood group was B Rh Positive.

Follow up ultrasound on Day 1 following birth; still demonstrated elevated fetal Middle Cerebral Artery-Peak Systolic Velocity in absence of fetal anemia. Plain Radiograph of Chest Antero Posterior view [CXR-AP] showed cardiomegaly [Table/Fig-3]. Heart size on the chest radiograph was larger than normal (cardiothoracic ratio > 0.65). Cardiac ultrasound demonstrated asymmetric septal hypertrophy [12 mm] and

marked concentric left ventricular hypertrophy [Table/Fig-4], indicative of Hypertrophic Cardiomyopathy. He was put on intravenous injection Lasix 3 mg every 8 hourly, i.v. Dopamine and Dobutamine @ 10-15 µl/kg/hour and Tablet Propranolol 2.5 mg every 12 hourly. Over the next few days his bluish body tinge and pan systolic murmur disappeared. Pulse Oximeter demonstrated a saturation of 92-96% without oxygen.

Repeat CXR – AP on Day 10 of life showed reduced and normalized size of cardiac silhouette [Table/Fig-5] and ultrasound [Table/Fig-6] demonstrated reduced thickening of interventricular septum [6 mm] as well as the left ventricle. Middle Cerebral Artery-Peak Systolic Velocity of the neonate [Table/Fig-7] demonstrated reduction in the values [28cm/s] as compared to the intrauterine measurement. The pattern of waveform too resembled a normal third trimester type waveform i.e. KG Type IC as per the Kachewar Gandage classification system for types of fetal Middle Cerebral Artery velocity waveform patterns [7].

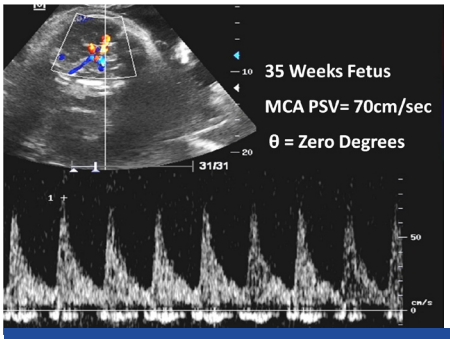
As the neonate was hale and hearty, he was discharged and called for follow-up every 3 months for the upcoming year. Thus, in this case the diagnosis of Hypertrophic Cardiomyopathy was reached on imaging studies that backed the clinical findings and it was postulated that increased velocity of blood ejected in the aorta due to increased left ventricular contractility in the setting of Hypertrophic Cardiomyopathy and not fetal anemia was responsible for the rise in fetal Middle Cerebral Artery-Peak Systolic Velocity values.

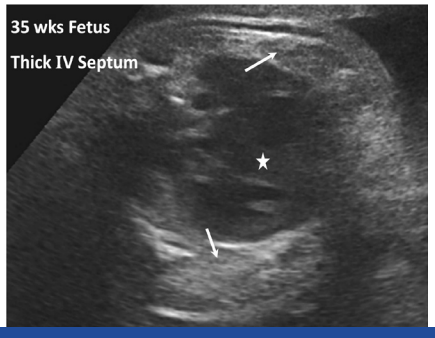
DISCUSSION

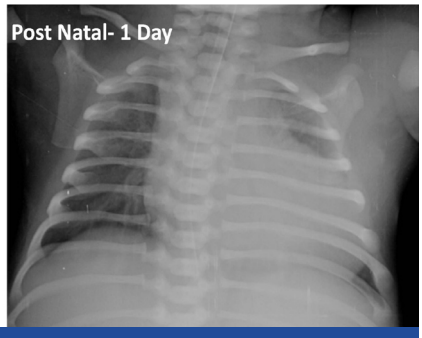
Several studies [1-5] across the globe have proved it time and again that by measuring the peak of the systolic velocity of fetal Middle Cerebral Artery waveform as seen on colour Doppler, a non-invasive diagnosis of fetal anemia can be reached. Infact, severe fetal anemia can be reliably diagnosed if this raised fetal Middle Cerebral Artery-Peak Systolic Velocity values are 1.5 times the Multiples of Median (MoM) value for that particular gestational age (GA) of the fetus. It is believed that the low viscosity of the fetal blood when it is anemic, due to any cause; leads to an increase in the cardiac output which ultimately manifests as raised peak velocity.

Apart from a rare case report [6] describing alpha thalassemia as a possible cause of raised fetal Middle Cerebral Artery-Peak Systolic Velocity in the absence of fetal anemia, no other causes have been documented to the best of our knowledge.

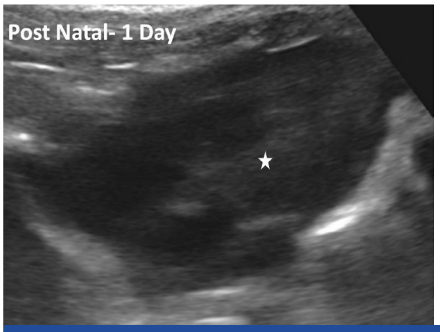
Hence we report this curious case of an infant of a diabetic mother, who during the intranatal period as well as during the early period following birth had elevated Middle Cerebral Artery-Peak Systolic Velocity more than 1.5 times the MoM

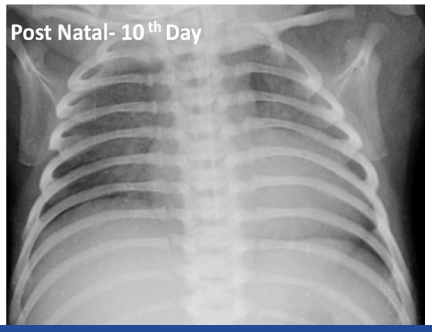


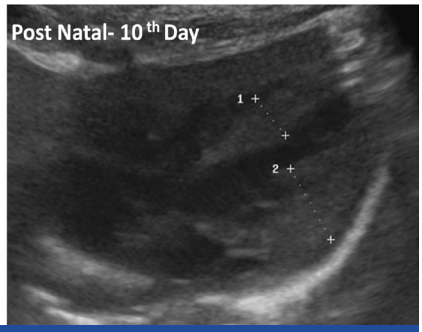




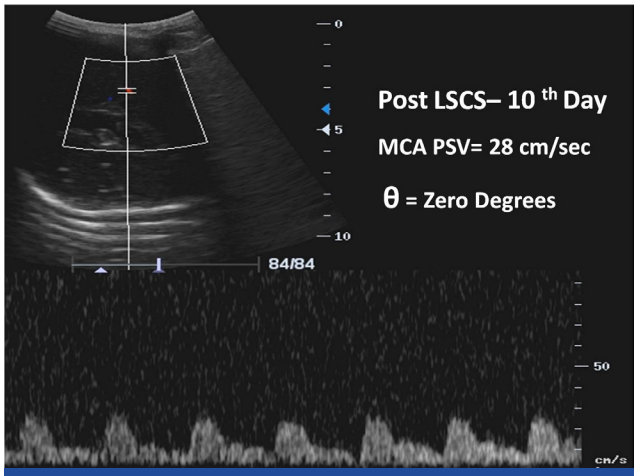
[Table/Fig-1]: Color Doppler Ultrasound showing raised Fetal MCA-PSV in 35 Weeks Fetus
[Table/Fig-2]: Grey Scale Ultrasound showing axial section of thorax of 35 Weeks Fetus. Thickening of soft tissues of thorax (arrows) and thickened interventricular septum (*) are seen
[Table/Fig-3]: Day 1-CXR-AP. Chest X-ray showing significant cardiomegaly (cardiothoracic ratio > 0.65). Hypertrophic cardiomyopathy in an infant of diabetic mother







[Table/Fig-4]: Day 1 - Grey Scale Ultrasound showing axial section of thorax. Thickened interventricular septum (*) and left ventricle are still seen
[Table/Fig-5]: Day 10-CXR-AP shows reduced size of cardiac silhouette with a normal cardio- thoracic ratio < 0.65
[Table/Fig-6]: Day 10 - Grey Scale Ultrasound of axial section of thorax showing reduced thickening of interventricular septum and left ventricle



[Table/Fig-7]: Color Doppler Ultrasound of neonatal head showing normalized MCA-PSV at 10 Days after Birth

value for that particular GA; and yet was non anemic. The raised MCA-PSV values ultimately normalized by the tenth day of birth. Hypertrophic Cardiomyopathy that is known to occur in the fetus of a diabetic mother was found to be the cause of this curious occurrence.

A global search for a non-invasive method to determine fetal anemia zeroed in on the utility of measuring the fetal Middle Cerebral Artery-Peak Systolic Velocity. Replication of this method was found to be simple, efficient as well as reliable and hence has been widely accepted [1-4] and is being actively practised. Off late, loco-regional differences between the standard values for each geographic locality have been described [2-6]. The shape as well as the pattern of MCA waveform also aid in diagnosing fetal hypoxia usually due to fetal anemia as has been described by Type III waveforms in the Kachewar Gandage classification system for types of fetal Middle Cerebral Artery velocity waveform patterns [7].

The lowered viscosity of anaemic blood coupled with increased cardiac output to maintain adequate oxygen, at least to vital organs results in elevated fetal Middle Cerebral Artery-Peak Systolic Velocity [1] and Type III Middle Cerebral Artery waveforms [2] when the fetal haemoglobin is reduced. The increase in this Middle Cerebral Artery-Peak Systolic Velocity beyond 1.5 times MoM is indicative of severe fetal anaemia [1, 2, 4].

Anemia in a fetus occurs when there is an inadequate number or quality of red blood cells in the fetal circulatory system. Hemolytic causes of fetal anemia can be grouped into Immune related disorders like Rh- Isoimmunization, ABO and Anti Kell Antibodies. Non Immune hemolytic causes include Red Cell Enzyme or Membrane Deficiency. Fetal anemia may also occur due to blood loss as in Fetomaternal Hemorrhage or Twin-twin transfusion. Miscellaneous conditions like Placental Chorioangioma and Congenital Infections like Parvovirus B19 or Cytomegalovirus too can cause fetal anemia. All these conditions can ultimately manifest as elevated fetal Middle Cerebral Artery-Peak Systolic Velocity.

There is a rare case report [6] describing an abnormal increase in fetal Middle Cerebral Artery-Peak Systolic Velocity without anemia on cordocentesis; even when Hydrops was present in a fetus with alpha-thalassemia. This is because HbBarts that is present in such patients has high affinity for oxygen which therefore prevents its release at tissue level; thereby inducing relative hypoxia. In order to compensate for this, cardiac output is increased as well as the peripheral resistance is reduced in Middle Cerebral Artery and this ultimately manifests as increased fetal Middle Cerebral Artery-Peak Systolic Velocity. Thus the amount as well as type of Hb; both determines the manifestation of anemia and Middle Cerebral Artery-Peak Systolic Velocity changes [7]. Cardiomegaly and elevated intracardiac blood velocities, along with elevated Middle Cerebral Artery Doppler flow, as an indirect result of increased cardiac output, was detected. Multiple logistic regression analysis revealed that both fetal hemoglobin and oxygen content were the factors that contributed to the increase in the Middle Cerebral Artery-Peak Systolic Velocity [7].

To the best of our knowledge, abnormally elevated fetal Middle Cerebral Artery-Peak Systolic Velocity and the occurrence of Kachewar Gandage Type III waveforms have never been reported without fetal anemia. The present case report is the first to successfully document that elevation of fetal Middle Cerebral Artery-Peak Systolic Velocity is possible due to cardiomyopathy that sometimes leads to enhanced left ventricular contractility which pumps more blood in the aorta with increased force that ultimately manifests as abnormal increase in the fetal Middle Cerebral Artery-Peak Systolic Velocity.

There is an increased risk of Hypertrophic Cardiomyopathy in infants of diabetic mothers [8, 9]. Such infants usually present with cardio respiratory distress and a disproportionate septal hypertrophy. The spectrum of Hypertrophic Cardiomyopathy can vary and may manifest as an incidental finding on echocardiography or as congestive heart failure. It has been reported that symptomatic Hypertrophic Cardiomyopathy occurs in 12.1% of infants of diabetic mothers and echocardiography surveillance has placed this figures at 30%. Initially, the left ventricular mass and contractility are increased [10, 11]. Maternal hyperglycemia during the third trimester leads to fetal hyperinsulinemic, anabolic status, the result of which manifests as hypertrophy of septum as well as ventricular wall.

Fetuses of diabetic mothers, who are diagnosed to have cardiomyopathy, in some cases demonstrate normal or slightly increased cardiac systolic function that manifests as slightly increased doppler velocity through the aorta. Hypertrophic Cardiomyopathy is usually benign and manifests clinically as systolic murmur and transitory cardiomegaly. All symptoms usually regress spontaneously within a few weeks. Sometimes, overt congestive heart failure develops, and is seen along with tachypnea, tachycardia, gallop rhythm and hepatomegaly [10, 11].

All surviving cases with maternal diabetes have been found

to progressively normalize after 3–6 months. This explains the finding of raised Middle Cerebral Artery-Peak Systolic Velocity that was seen in utero and in early neonatal period in the present case that eventually normalized by day 10. Like in a reported study [9], present study too had asymmetric left ventricular hypertrophy and a nondilated left ventricle as the hallmark of HOCM. Echocardiography in Hypertrophic Cardiomyopathy demonstrates intraventricular septum thickening of mean 4.77 mm when compared with those born to non-diabetic mothers 2.5 mm [11].

As the natural history of Hypertrophic Cardiomyopathy is that of spontaneous regression of symptoms and septal hypertrophy, supportive care, with fluid restriction, diuretics and oxygen, help such neonates to tide over this crisis [9, 10]. Digoxin and inotropes are contraindicated as they increase left ventricular outflow tract obstruction. Beta adrenergic blocking agent like propranolol is found to be very effective as it decreases heart rate, left ventricular contractility and wall stress, and a total relief of symptoms has been reported in 30% of affected infants. Surgery has a role only when the septal hypertrophy and outflow tract obstruction cause significant symptoms despite medical therapy. Catheter alcohol ablation and surgical septal myotomy or myomectomy are some of the options. It is also believed that the severity of Hypertrophic Cardiomyopathy can be reduced by, appropriate diabetic management in every pregnancy itself.

CONCLUSION

All fetuses with abnormally elevated fetal Middle Cerebral Artery-Peak Systolic Velocity values do not necessarily have fetal anemia. Hypertrophic Cardiomyopathy in the fetus as well as a neonate of a diabetic mother too can give rise to raised fetal Middle Cerebral Artery-Peak Systolic Velocity values. This elevation is temporary and normalizes as soon as the Hypertrophic Cardiomyopathy regresses. An active search should therefore be carried out in all fetuses that have abnormally elevated fetal Middle Cerebral Artery-Peak Systolic Velocity so as to label them as severly anemic, but have no anemia on cordocentesis; to find underlying cardiac abnormalities like Hypertrophic Cardiomyopathy for earlier diagnosis and timely management.

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