Case Report

Middle Cerebral Artery Peak Systolic Velocity in Fetuses with Homozygous Alpha-Thalassemia-1: Case Series

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Objectives: *The objective of this study is to evaluate the potential usefulness of middle cerebral artery peak systolic velocity (MCA-PSV) as a non-invasive means of detecting an anemic fetus from homozygous alpha-thalassemia-1*

Material and Method : *We observed four cases of referrals with complicated pregnancies in which the fetuses were suspected with homozygous alpha-thalassemia-1. Three out of four cases involved hydrop fetalis, detected through previous ultrasounds, while the remaining case was referred for prenatal diagnosis. Subsequently, we performed a detailed ultrasound and fetal MCA-PSV in all cases, and to confirm the diagnosis, we also performed cordocentesis.*

Results: *With all the four cases having the gestational age range from 18 to 27 weeks, three showed hydrop fetalis. The remaining case, the 18-week gestational age fetus referred for prenatal diagnosis, showed an increase in the cardiothoracic ratio without other signs of hydrop fetalis. MCA-PSV suggested the presence of fetal anemia in all cases (with the velocity ranging from 37.3 to 62.2 cm/sec). The results obtained from cordocentesis confirmed fetal anemia and homozygous alpha-thalassemia-1 in all cases.*

Conclusion: *Peak systolic velocity of fetal middle cerebral artery can predict anemia in fetus affected with homozygous alpha-thalassemia-1 disease.*

Keywords*: Thalassemia, Hydrops, Middle cerebral artery peak systolic flow, Fetal anemia*

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In Southeast Asia, 60-90% of hydrops fetalis have been reported to be caused by homozygous alpha-thalassemia-1 or Hb Bart's hydrops fetalis[1-4]. Clinical features of these infants may involve pallor, slight jaundice, growth restriction, edema, distended abdomen from hepatosplenomegaly and ascites. The placenta is greatly enlarged and friable. Furthermore, common obstetric complications are frequently seen in affected pregnancies, including preeclampsia, antepartum hemorrhage, preterm labor, dystocia and postpartum hemorrhage[1-4]. Pregnant women and her families also suffer from carrying a nonviable fetus.

At the antenatal clinic of Department of Obstetrics and Gynecology, HRH Princess Maha Chakri Sirindhorn Medical center, Faculty of Medicine, Srinakharinwirot University, a routine screening program is performed to detect both a carrier and couple at risk for severe thalassemia fetus. For all couples at risk for severe thalassemia fetus, both in-patients and referrals from other hospitals, we perform genetic counseling and gave information regarding prenatal diagnosis option available. A prenatal diagnosis was done mostly by cordocentesis. Ultrasound monitoring is selected as a non-invasive means of detecting fetal at risk for homozygous alpha-thalassemia-1. We also performed cordocentesis to confirm the diagnosis when

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abnormal sonographic finding is detected.

While middle cerebral artery peak systolicing velocity (MCA-PSV) has been commonly used as a non-invasive indicator for detecting an anemic fetus with alloi-mmunization, this condition is rare in our country because the prevalence of Rhesus D-negative among Thai people is less than 1%. Hypothesizing that this method may help to detect early evidence of fetal anemia involving homozygous alpha-thalassemia-1 before anatomical changes occur, we have decided to add this diagnostic method to our thalassemia control program.

Material and Method

Ultrasound assessments are performed to all pregnant women who are at risk for homozygous alpha-thalassemia-1 fetus starting from 15 weeks of gestation and also for the referral cases during the initial visit. For this study, we observed four cases of referrals with complicated pregnancies in which the fetuses were suspected to have homozygous alpha-thalassemia-1. Three out of four cases involved hydrop fetalis, detected through previous ultrasounds assessment, while the remaining case was referred to us for prenatal diagnosis.

A detail ultrasound was performed for each case, including an anatomical survey, the cardiothoracic ratio, placental thickness, hydropic change, umbilical vein dilatation[5] and fetal MCA-PSV. An MCA-PSV measurement after the transverse section of the fetal head is obtained at the level of sphenoid bones. The circle of Wilis is identified by color Doppler. Adjust until get an angle of zero degree between the ultrasound beam and the direction of blood flow. A sample cursor was placed at the center of the vessel closed to its origin from the internal carotid artery. Measurement was repeated at least three times in each fetus[6,7]. Subsequently, cordocentesis was performed, and fetal blood analysis was done with a complete blood count and high-performance liquid chromatography to confirm the diagnosis.

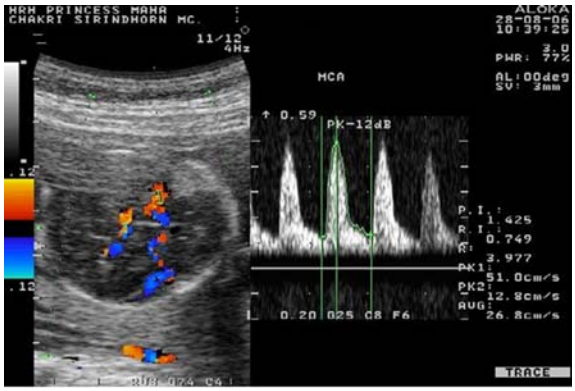

Fig. 1 Color Doppler ultrasound image showing the middle cerebral artery peak systolic velocity (MCA-PSV) of the second case.

Results

With all the cases having the gestational age range between 18 to 27 weeks, three of the cases had been diagnosed with previous homozygous alpha-thalassemia-1 fetus and three of the cases exhibited hydrop fetalis. In contrast, the 18-week fetus that referred for prenatal diagnosis showed an increase in the cardiothoracic ratio without sign of hydrop fetalis. The MCA-PSV suggested the presence of fetal anemia in all cases (with the rate ranging from 37.3 to 62.2 cm/sec). All cases had MCA-PSV above the reference range of 1.5 multiple of the median. The results obtained from cordocentesis confirmed fetal anemia and homozygous alpha-thalassemia-1 in all cases. Clinical details were shown in Table 1.

Discussion

Ultrasound findings of homozygous alpha-

Table 1. Clinical details of the four pregnant women with homozygous alpha-thalassemia-1 fetus

Case	GA (week)	Gravida/ Previous Bart	Hydropic change	Cardiothoracic ratio	MCA-PSV (cm/sec)	Hct / Hb
1	27	1 / No	Yes	Marked increase	62.2 (52.8)*	27.1 / 6.9
2	18	3 / Yes	No	0.61	51.0 (34.8)*	24.4 / 5.7
3	25	3 / Yes	Yes	Marked increase	56.7 (48.2)*	23.6 / 6.6
4	18	6 / Yes	Yes	Marked increase	37.3 (34.8)*	22.0 / 5.3

* 1.5 MoM MCA-PSV from Mari 2005, MCA-PSV: middle cerebral artery peak systolic velocity

thalassemia-1 at midpregnancy are the increase in the cardiothoracic ratio and placental thickness, dilated umbilical vein and hydropic change. The most sensitivity marker is the cardiothoracic ratio, followed by increased placental thickness. Hydropic change, on the other hand, is the most specific marker[5]. Sonographic markers are used in many institutes as a noninvasive method to diagnose homozygous alpha-thalassemia-1 fetus before an invasive procedure is called for, this protocol can effectively decrease unnecessary invasive prenatal diagnostic procedures for non-disease fetuses. A late diagnosis is a disadvantage of the follow-up ultrasonography protocol.

Severe fetal anemia was detected after birth in these fetuses with a mean hemoglobin level of 6.5 g/dL[8]. Theoretically, fetal anemia probably develops around 6-7 weeks' gestation when the switch from embryonic to fetal hemoglobin gene expression occurs[9]. MCA-PSV is commonly used as a non-invasive marker to detect an anemic fetus with alloimmu-nization, parvovirus B19, massive fetomaternal hemorrhage, homozygous alpha-thalassemia-1 and twins-to-twins transfusion syndrome[10-16]. MCA-PSV is thus a good marker for detecting moderate to severe anemic fetus, not in mild cases[6]. This marker may as well be use as a non-invasive marker of choice for detecting anemic fetus from homozygous alpha-thalassemia-1 before anatomical changes occur.

Our findings confirm the results obtained in a previous study. Peak systolic velocity of fetal middle cerebral artery can predict anemia in fetus affected with homozygous alpha-thalassemia-1 disease. This study also showed various degree of expression of homozygous alpha-thalassemia-1 that every sonographers should be aware of when ultrasound strategy is used. However, a further study about the efficacy of this marker especially in early gestational age is recommended.

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Middle Cerebral Artery Peak Systolic Velocity ของทารกในครรภ์ที่เป็น *Homozygous Alpha-Thalassemia-1:* ชุดผู้ป่วย

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วัตถุประสงค์*: ศึกษาประโยชน์ของการใช้ middle cerebral artery peak systolic velocity (MCA-PSV) ในการค้นหาทารกในครรภ์มารดาที่มีภาวะซีดจาก homozygous alpha-thalassemia-1*

วัสดุและวิธีการ*: หญิงตั้งครรภ์ 4 รายที่ได้รับการส่งตัวมารับการตรวจวินิจฉัยก่อนคลอด (prenatal diagnosis) หาภาวะ homozygous alpha-thalassemia-1 ของทารกในครรภ์ มี 3 รายที่ได้รับการส่งตัวมาเนื่องจากทารกในครรภ์มีอาการบวมน้ำจากการตรวจด้วยคลื่นเสียงความถี่สูง ส่วนอีก 1 รายส่งตัวมาเพื่อรับการตรวจวินิจฉัยก่อนคลอด เนื่องจากเป็นคู่เสี่ยงที่มีโอกาสมีทารกในครรภ์เป็น homozygous alpha-thalassemia-1 ทุกรายได้รับการสืบค้น เพิ่มเติมด้วยคลื่นเสียงความถี่สูงเพื่อสำรวจ โครงสร้างของทารกในครรภ์โดยละเอียด ร่วมกับการตรวจ MCA-PSV หลังจากนั้นจึงทำ cordocentesis เพื่อยืนยันผลการวินิจฉัย*

ผลการวิจัย*: หญิงตั้งครรภ์ทั้ง 4 ราย มีอายุครรภ์ตั้งแต่ 18 ถึง 27 สัปดาห์ มี 3 รายที่ตรวจพบว่าทารกในครรภ์มีภาวะ hydrop fetalis ส่วนอีก 1 รายที่ได้รับการส่งตัวมาเพื่อรับการตรวจวินิจฉัยก่อนคลอดเนื่องจาก เป็นคู่เสี่ยงที่มีโอกาสมีทารกในครรภ์เป็น homozygous alpha-thalassemia-1 มีอายุครรภ์ 18 สัปดาห์ตรวจพบว่ามี cardiothoracic ratio เพิ่มขึ้นเพียงอย่างเดียวโดยไม่มีภาวะ hydrop fetalis ระดับ MCA-PSV ที่วัดได้ทำให้สงสัยภาวะซีดของทารกในครรภ์ทุกราย (MCA-PSV มีค่าอยู่ระหว่าง 37.3 ถึง 62.2 cm/sec) ผลการตรวจเลือดของทารกในครรภ์ที่ได้จากการทำ cordocentesis ยืนยันภาวะซีดและ homozygous alpha-thalassemia-1 ของทารกในครรภ์ทุกราย*

สรุป*: MCA-PSV มีประโยชน์ในการวินิจฉัยภาวะซีดจาก homozygous alpha-thalassemia-1 ของทารกในครรภ์*
