Case Report

An Increase of the Cardiothoracic Ratio Leads to a Diagnosis of Bart's Hydrops

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Background: *Thalassemia is a common single gene disorder in Southeast Asia. α-thalassemia is a group of syndrome characterized by deficient production of the α-globin chain. Individuals with heterozygous α-thalassemia-1 are at risk of having a fetus that has Hemoglobin Bart's hydrops fetalis (Hb Bart's). Usually, when the hemoglobin electrophoresis in heterozygous α-thalassemia-1 is normal, the Mean Corpuscular Volume (MCV) is lowered. We report a case of increased cardiothoracic ratio that led to a diagnosis of Hb Bart's in a couple who had normal hemoglobin electrophoresis and low MCV.*

Case Report: *A 23-year-old woman, gravida 2, Para 0-0-1-0, initially presented for antenatal care at 13 weeks pregnancy. Her MCV was 67 fentolitre, DiChlorophenol-IndolPhenol (DCIP) test was negative and hemoglobin electrophoresis was normal. Her husband's MCV was 67 fentolitre, and hemoglobin electrophoresis was normal. Cardiomegaly (an increased of the cardiothoracic ratio) was detected by ultrasonogram at 25 weeks of gestation. She and her husband were comprehensively counseled after an Hb Bart's was suspected. A cordocentesis was performed and the fetal blood was tested for hemoglobin electrophoresis. The result was later known and confirmed as Hb Bart's. The couple decided to terminate the pregnancy. The induced abortion was successful and the patient was discharged on the second day after the abortion. She was well at the 4-week follow-up.*

Conclusion: *A prenatal ultrasonographic screening should be conducted in couples who are suspected of being α-thalassemia-1 carriers when DNA study of α-globin gene cannot be performed. The increase of cardiothoracic ratio will help detect an early stage of Hb Bart's.*

Keywords: *Cardiothoracic ratio, Hemoglobin Bart's, Hydrops fetalis, Alpha thalassemia*

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Thalassemia is one of the most common single gene disorders in the world. The greatest frequencies are recognized in areas where falciparum malaria was endemic, including the Mediterranean, Southeast Asia, the Arabian Peninsula, Turkey, Iran, west and central Africa, India, and the Pacific Islands[1]. Thalassemia is an inherited disorder of hemoglobin production. Hemoglobin is composed of two α chains and two β chains. A decrease in the synthesis of α chains causes α-thalassemia and β chains causes β-thalassemia. The frequency of α-thalassemia reaches 20-30% in Bangkok and Northern Thailand and the frequency of β-thalassemia varies between 3 and 9% [2].

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There are four α globin genes, two copies on each chromosome 16. The normal α globin gene compliment is designed αα/αα. Individuals who carry deletions of two a globin genes on the same chromosome have α-thalassemia-1 haplotype (--/-), also known as cis deletion or α^0-thalassemia mutation. Those who carry two deletions on opposite chromosomes have α-thalassemia-2 haplotype (-α/), or α^+-thalassemia. The prevalence of α-thalassemia-1 and α-thalassemia-2 in Thailand were both 10%[3]. A deletion of four α globin genes (--/--) causes hemoglobin Bart's hydrops fetalis. The fetus cannot synthesize α globin chain, which results in severe hemolytic anemia and hypoxia from early fatal life. Perinatal fetal death is the usual

outcome and the obstetric complications in women carrying an affected pregnancy are common. If both parents are carriers of α^0-thalassemia haplotype, there is a 25% risk for the fetus to be affected with Hb Bart's[1]. Prenatal diagnosis is achieved by DNA studies for all at-risk pregnancies. Thus, screening test for a carrier of α^0-thalassemia haplotype is essential in antenatal care. Herein, The authors report a case of increased cardiothoracic ratio which led to a diagnosis of Hb Bart's in whom α-thalassemia-1 carriers was not detected.

Case Report

A 23-year-old woman, gravida 2, Para 0-0-1-0, initially presented for antenatal care at 13 weeks of pregnancy on February 22, 2005. She had morning sickness. Physical examination at her first antenatal visit revealed a blood pressure of 110/60 mmHg, pulse rate of 80/min and respiratory rate of 20/min. Her height and weight were 156 cm and 38.5 kg, respectively. Her uterine size was consistent with 13 weeks pregnancy. Her initial blood tests included a hematocrit of 33%, mean corpuscular volume (MCV) of 67 fentolitre, white blood cell count of 8,500 cells/mm^3 with 68.7% neutrophils, and platelets of 309,000/mm^3. The VDRL was non-reactive, HBsAg negative and anti HIV negative. Her dichlorophenol-indolphenol (DCIP) test was negative. Her hemoglobin electrophoresis was normal. Her husband also received a blood test. His hematocrit was 40.9%, MCV was 67 fentolitre, and hemoglobin electrophoresis was normal. She was prescribed antenatal vitamin and folic acid. She had regular and unremarkable antenatal care.

At 25 weeks of gestation, ultrasonogram was performed to check the fetus. The result revealed a single viable fetus compatible with 25 weeks pregnancy. Cardiomegaly was detected by increased cardiothoracic ratio (0.7) (Fig. 1). The placental thickness was 59 mm. The couple were comprehensively counseled on the ultrasonographic findings that early sign of Bart's was suspected. Cordocentesis was performed and the fetal blood was sent for hemoglobin electrophoresis. The result was confirmed as Hb Bart's.

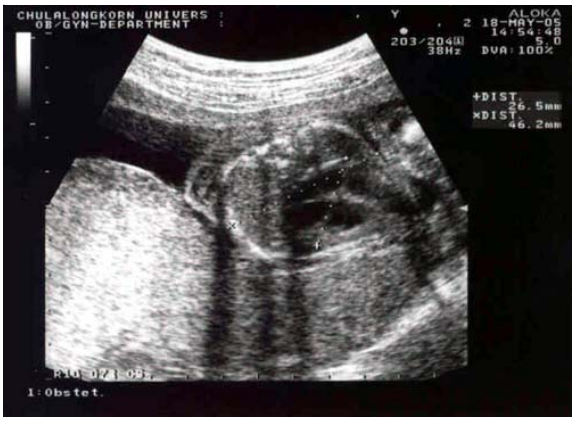

Fig. 1 Transabdominal ultrasonogram demonstrated an increased of fetal cardiothoracic ratio

Based on the result, the couple decided to terminate the pregnancy. An induced abortion with vaginal misoprostal 200 micrograms every six hours was initiated. A male abortus was aborted seven hours later without maternal complication. At the postabortion examination, the body weighed 800 grams. No gross abnormalities were detected. The patient was discharged on the second day postabortion. She was well at the 4-week follow-up. She and her husband were counseled on the 25% chance of recurrence of the disease and possibilities of prenatal diagnostic methods.

Discussion

The present case is a case of increased fetal cardiothoracic ratio that leads to a diagnosis of Hb Bart's hydrops fetalis in a couple who have normal hemoglobin electrophoresis and low MCV.

The case confirmed that a normal result of hemoglobin electrophoresis could not rule out α-thalassemia carrier[1]. Thus, in an area where DNA studies are available, couples who have normal hemoglobin electrophoresis and low MCV should seek further evaluation of α-globin genes mutation as recommended by the American College of Obstetricians and Gynecologists (ACOG). As seen in this case, individuals who have heterozygous α-thalassemia-1 (--/$\alpha\alpha$) are at risk of having a fetus that has Hb Bart's.

The author use MCV and DCIP test for screening of thalassemia carriers in pregnant women[4]. When either MCV or DCIP test is abnormal, hemoglobin electrophoresis of the couple is performed. If the hemoglobin electrophoresis of the couple is abnormal, they have a significant risk to have a fetus who has a significant hemoglobinopathy, prenatal diagnosis should be offered[4]. The most accurate test is direct DNA analysis.

Prenatal diagnosis is conventionally achieved by performing chorionic villus sampling or amniocentesis or cordocentesis and DNA studies or cordocentesis and hemoglobin electrophoresis for all at-risk pregnancies wherever available. These procedures carry a small risk (0.5-3.7%) to the fetus[4].

Lam et al reported a safer prenatal diagnostic method, i.e., the measurement of cardiothoracic ratio for the prediction of Hb Bart's at gestational age 12-13 weeks. The rational was that fetuses affected by type 1 homozygous α-thalassemia have deficient a-globin synthesis. Because α-globin-dependent hemoglobin F becomes the major fetal hemoglobin from 8 weeks of gestation, they assume that the affected fetuses are anemic in the first trimester of pregnancy. In response to the anemia and hypoxia, the fetus tries to compensate by dilating the cardiac chamber and increasing cardiac output. The cutoff point of cardiothoracic ratio $\geq$ 0.5 give 100% sensitivity and specificity for the disease[5]. This test can avoid unnecessary invasive testing on unaffected fetuses. Thus, in settings where DNA studies are not readily available or the at-risk couples do not want to take any risk of invasive procedure, the use of prenatal ultrasonographic screening may be an alternative method for the prediction of Hb Bart's. When the ultrasonographic findings are abnormal, cordocentesis for hemoglobin electrophoresis should be performed.

In conclusion, where the DNA study of α-globin gene cannot be performed, the prenatal ultrasonographic screening should be performed in couples suspected of being α-thalassemia-1 carriers for early detection of Hb Bart's hydrops fetalis, which can be demonstrated by increased cardiothoracic ratio.

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การเพิ่มขึ้นของสัดส่วนของหัวใจต่อช่องอกนำไปสู่การวินิจฉัยทารกบวมน้ำชนิดฮีโมโกลบิน Bart's

วรพงศ์ ภู่พงศ์

อัลฟาธาลัสซีเมียเป็นความผิดปกติของยีนเดี่ยวที่พบบ่อยในเอเชียตะวันออกเฉียงใต้รวมทั้งประเทศไทย อัลฟาธาลัสซีเมียเป็นกลุ่มอาการที่เกิดจากการลดลงของการสร้างสายอัลฟาโกลบิน คู่สมรสที่เป็นพาหะของอัลฟาธาลัสซีเมีย-1 มีความเสี่ยงที่ทารกในครรภ์จะเป็นฮีโมโกลบิน Bart's โดยปกติการตรวจฮีโมโกลบินอิเลคทรอฟอเรซิสในพาหะของอัลฟาธาลัสซีเมีย-1 ผลจะปกติ แต่ขนาดเม็ดเลือดแดงจะเล็กลง ผู้รายงานได้รายงานทารกที่มีการเพิ่มขึ้นของสัดส่วนของหัวใจต่อช่องอกนำไปสู่การวินิจฉัยทารกบวมน้ำชนิดฮีโมโกลบิน Bart's ในคู่สมรสที่มีฮีโมโกลบินอิเลคทรอฟอเรซิสปกติ และมีขนาดเม็ดเลือดแดงเล็ก ผู้ป่วยหญิงอายุ 23 ปีตั้งครรภ์ครั้งที่ 2 เคยแท้ง 1 ครั้งมาฝากครรภ์ครั้งแรกเมื่ออายุครรภ์ 13 สัปดาห์ พบว่าเม็ดเลือดแดงมีขนาด 67 เฟมโตลิตรและผลตรวจ DCIP ปกติ ผลการตรวจฮีโมโกลบินอิเลคทรอฟอเรซิสปกติ ผลการตรวจเม็ดเลือดแดงของสามีมีขนาด 67 เฟมโตลิตร และผลการตรวจฮีโมโกลบินอิเลคทรอฟอเรซิสปกติ ได้ทำการตรวจอัลตราซาวด์เมื่ออายุครรภ์ 25 สัปดาห์พบว่าทารกในครรภ์มีขนาดหัวใจโต (มีการเพิ่มขึ้นของสัดส่วนของหัวใจต่อช่องอก) คู่สมรสได้รับคำปรึกษาถึงผลการตรวจที่พบว่าเป็นสิ่งตรวจพบของทารกบวมน้ำชนิดฮีโมโกลบิน Bart's ได้ทำการเจาะเลือดจากสายสะดือของทารกในครรภ์ เพื่อตรวจฮีโมโกลบินอิเลคทรอฟอเรซิส ซึ่งผลยืนยันว่าเป็นฮีโมโกลบิน Bart's คู่สมรสได้ตัดสินใจขอยุติการตั้งครรภ์ และได้ทำการยุติการตั้งครรภ์โดยไม่มีภาวะแทรกซ้อน ผู้ป่วยสามารถกลับบ้านได้วันที่ 2 หลังยุติการตั้งครรภ์และปกติดีเมื่อมาตรวจติดตามที่ 4 สัปดาห์ โดยสรุปในสถานที่ที่ไม่สามารถตรวจอัลฟาโกลบินยีน ควรทำการตรวจอัลตราซาวด์ทารกในครรภ์ในคู่สมรสที่สงสัยว่าจะเป็นพาหะของอัลฟาธาลัสซีเมีย-1 เพื่อที่จะตรวจหาทารกบวมน้ำชนิดฮีโมโกลบิน Bart's ได้เร็วขึ้นโดยจะพบการเพิ่มขึ้นของสัดส่วนของหัวใจต่อช่องอก