
OBSTETRICS

Prenatal Diagnosis of Alpha Thalassemia : Using Ascitic or Pleural fluid as a source for DNA Analysis

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ABSTRACT

Hydrops fetalis means an excess of total body water, which accumulates extra cellularly and in serous cavity of the fetus. The fetal ascitic and pleural fluid were known to be contained fetal lymphocytes. To evaluate the cause of the hydrops fetalis, DNA analysis and karyotyping can be successfully done from the fetal ascitic and pleural fluid. We reported two cases of Hydrops fetalis :

Case 1. Hb Bart's hydrops fetalis diagnosed by DNA amplification using the PCR technique, performed on the fetal ascitic fluid.

Case 2. Idiopathic Hydrops fetalis diagnosed on the basis of normal karyotype and DNA analysis, performed on the fetal pleural fluid.

Key word : hydrops fetalis, prenatal diagnosis, DNA analysis.

The latin term "Hydrops Fetalis" refers to pathologically increased fluid accumulation in serous cavities or edema of soft tissue in a fetus. It is generally classified into immune and non-immune types. Immune Hydrops is primarily due to incompatibility of maternal antibodies with Rhesus (Rh) antigens on fetal red cells. Rh isoimmunization can occur when the mother is Rh negative and the fetus is Rh positive.

Non-immune Hydrops fetalis causes by various etiologies, other than blood group incompatibility. The non-immune Hydrops fetalis is a heterogeneous disorder resulting from a wide variety of underlying etiologies, that originated from fetal or maternal or placental or unknown etiology.⁽¹⁾ The most common cause of Hydrops fetalis in Thailand is non-immune type causes by fetal Hb Bart's hydrops (Alpha Thalassemia). The mother

who carries the fetus with Hb Bart's Hydrops will suffered from obstetric complications such as pregnancy induce hypertension mostly severe form, antepartum haemorrhage and postpartum haemorrhage. The other conditions that causes non-immune hydrops fetalis are cardiovascular and pulmonary abnormalities, chromosomal abnormalities, infection, neoplastic and liver disorder. The clinical outcome of fetus with non-immune hydrops fetalis can be predicted only when the correct etiology is identified.⁽²⁾ The fetal evaluation should be included both invasive and noninvasive. The useful step is to start with noninvasive procedure first, that is sonographic evaluation to ruled out associated fetal anomaly. The invasive fetal evaluations are DNA analysis and fetal karyotype to rule out the fetal Hb's Bart hydrops and fetal chromosome abnormality. The usual method is to perform the amniocentesis for chromosome analysis which will take 2-3 weeks before getting the result. The rapid karyotype can be performed by fetal blood sampling. However the fetal blood sampling must be performed by experienced physician and also need the expensive high resolution ultrasound machine. The fetal loss rate due to fetal blood sampling technique was known to be higher than the amniocentesis.⁽³⁾

The fetal ascitic and pleural fluid were known to be contained fetal lymphocytes. The rapid karyotype can be performed on the fetal ascitic and pleural fluid and will take only 72-96 hours before getting the result.⁽⁴⁾ The DNA analysis for prenatal diagnosis of Hb Bart's hydrops fetalis by polymerase chain reaction (PCR) technique. The Amniocytes in the amniotic fluid and the lymphocytes in the ascitic and pleural fluid were extracted and using three and four oligonucleotide primers were performed.⁽⁵⁾ The sampling technique for collecting the asitic

and pleural fluid is similar to the technique of amniocentesis under the ultrasound guidance, that is easier and does not need the expensive high resolution ultrasound machine when compare to the technique of fetal blood sampling. The complication of the procedur should be the same as the amniocentesis.

We reported two cases of non-immune hydrops fetalis that the fetal evaluation by rapid fetal karyotype and fetal DNA analysis were successful from the fetal ascitic and pleural fluid.

Case Report

1. A 25 years old gravida 2, para 1, woman was referred to the prenatal diagnostic unit, Pramongkutkla hospital for evaluation of hydrops fetalis. The ultrasound study showed single fetus with posterior enlarged placenta and decreased in amniotic fluid volume. The fetus showed enlarged abdomen with fluid surrounding the liver, bowel, extra hepatic portion of the umbilical vein and the falciform ligament. The fetal cardiac enlargement with pericardial effusion without evidence of fetal anatomical heart defect was demonstrated. No other abnormality of the fetus was detected by the ultrasonographic examination. The invasive fetal evaluation by amniocentesis and fetal ascitic fluid aspiration for chromosome and DNA analysis were performed. The results show normal karyotype and Hb Bart's hydrops fetalis (fig 1.)

The patient and her husband decided to terminate the pregnancy. The fetus was delivered with enlarge abdomen compatible with the clinical diagnosis of hydrops fetalis. The fetal heart blood was sent for Hb eletrophoresis and confirmed the diagnosis of Hb Bart's Hydrops fetalis (fig 2)

Case 2. A 28 years old primigravida

was referred to the prenatal diagnostic unit, Pramongkutkla Hospital for evaluation of hydrops fetalis. The ultrasound demonstrated with massive pleural effusion, generalized edema, minimal amount of ascitic fluid was noted. No other congenital defected was demonstrated

during the examination. The amniocentesis and pleural fluid aspiration were performed under ultrasound guidance. The amniotic and pleural fluid specimen were send to the laboratory for DNA analysis to ruled out Hb Bart's Hydrops fetalis and chromosome analysis. The result

CASE 1. DNA and Karyotyping

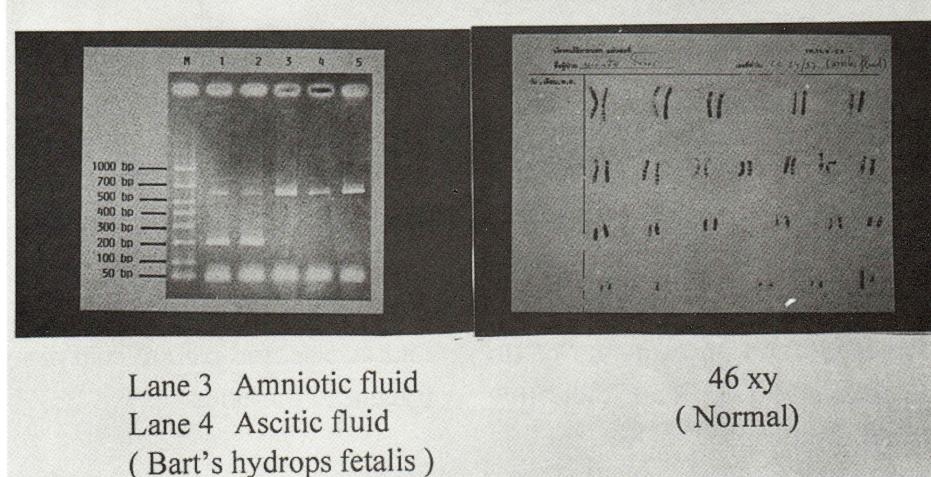


Fig. 1. DNA and Karyotyping from the fetal ascitic fluid.

CASE 1. Hb Electrophoresis (Bart's Hydrops fetalis)



Fig. 2. The fetus and the Hb electrophoresis.

CASE 2. DNA and Karyotyping

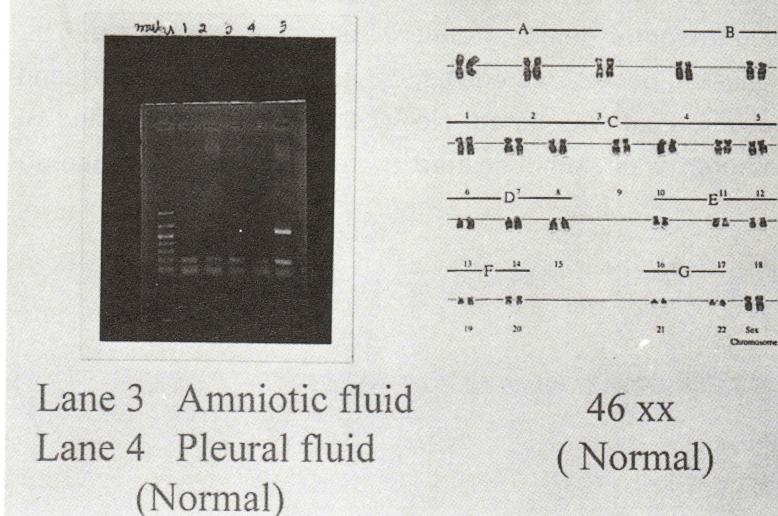


Fig. 3. DNA and chromosome from the amniotic and pleural fluid.

show normal karyotype and no evidence of Hb Bart's Hydrops fetalis (fig 3.) The idiopathic Hydrops fetalis was diagnoses.

The patient and husband decided to continue this pregnancy. The pregnancy continue to term and delivered the stillborn fetus.

Discussion

Pathogenesis of Hydrops fetalis is heterogeneous disorder resulting from a wide variety of underlying etiologies.⁽¹⁾ Prenatal evaluation to identify the cause is very important in planning the management and give prognosis of the fetus.

The pleural fluid and ascitic fluid can be another sources for DNA and chromosome analysis for prenatal diagnosis. This is very useful procedure in case of oligohydramnios with hydrops fetalis. The ascitic and pleural fluid contain fetal lymphocytes, so the rapid karyotype can be sucessful analyzed by standard method for fetal blood. The procedure for aspiration of

fetal ascitic and pleural fluid are simple and less trauma to the fetus.

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