CASE STUDY

Nonimmune hydrops fetalis

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Abstract

BACKGROUND: Nonimmune hydrops fetalis (NHF) is an abnormal accumulation of fluid – especially serous – in visceral cavities and soft tissues. This condition may be caused by: cardiovascular diseases, chromosomal disorders, infections, lung, stomach, intestinal, kidneys, urinary tract and blood diseases, metabolic disorders and tumors. NHF may by diagnosed by an ultrasound scan.
THE AIM of the study was to present diagnostic and therapeutic difficulties as well as management with reference to NHF.
CASE STUDY: An abnormal accumulation of fluid in visceral cavities and subcutaneous tissue of two fetuses was diagnosed by an ultrasound scan. Despite a detailed and specific diagnostic proceeding which included: infections, congenital malformations, chromosomal abnormalities etc. it was impossible to establish the cause of NHF. The symptomatic therapy was performed: periodic cordocentesis with an injection of human albumin solutions. In case of the first fetus therapeutic thoracocentesis was performed. The fetuses were delivered in 32nd and 31st week of pregnancy. Both neonates survived but even after the delivery it was impossible to establish the cause of NHF.
CONCLUSIONS: Multidirectional diagnostic approach is essential for the implementation of causal treatment of NHF. In case of idiopathic NHF the only management is symptomatic therapy, fetal monitoring and preterm delivery.

INTRODUCTION

Fetal hydrops is an abnormal accumulation of fluid – especially serous – in visceral cavities and soft tissues. In the past this condition was most often diagnosed in case of Rhesus (Rh) isoimmunization of the mother. Recently such cases have been occasional by reason of common prophylaxis consisting in anti-D immunoglobulin administration. However, the problem of nonimmune hydrops fetalis (NHF) caused by other reasons than Rh isoimmunization still remains. The cause of such condition may be as follows: cardiovascular diseases, chromosomal disorders, infections, lung, stomach, intestinal, kidneys, urinary tract and blood diseases, metabolic disorders and tumors. Nowadays, the high definition ultrasound machines make the diagnosis easy, however, a great diversity of possible causes of NHF still pose a diagnostic and therapeutic difficulty. Due to the NHF perinatologists are frequently impelled to induce a preterm labour in cases when continued gestation represents a higher risk for the fetus than a preterm delivery.

The aim of the study was to present, on the basis of two cases, diagnostic and therapeutic difficulties and management of NHF.

Abbreviations:
NHF – nonimmune hydrops fetalis
CMV – Cytomegalovirus
B19V – Parvovirus B19

CASES DESCRIPTION

First case

A 26-year old primigravida was admitted to the hospital in 19th week of pregnancy due to fetal pleural effusion diagnosed by an ultrasound scan. Moreover, the following was diagnosed: double vessel umbilical cord (one artery, one vein), normal amount of amniotic fluid, normal placental thickness (41 mm) and normal fetal anatomy. In the previous standard ultrasound scan conducted in 13th week of pregnancy – no abnormalities had been revealed (Czuba *et al.* 2007). The patient's medical history was insignificant and the results of routine blood tests were normal. Rh isoimmunization was excluded. Diagnostic proceeding was immediately implemented with the aim of establishing the causes of NHF. Toxoplasma gondii, Cytomegalovirus and Treponema pallidum infection were excluded. The alpha-fetoprotein level was within normal limits. Cervical culture and chlamydia tests were negative. Genetic amniocentesis was performed showing normal male karyotype. Due to an accumulation of fluid in pleural cavities of the fetus the diagnostic and therapeutic thoracocentesis were performed. The result of fluid culture was negative, chylothorax was excluded, no DNA indicating CMV, Toxoplasma or B19V infection was present. After interim recovery re-accumulation of the fluid in the pleural cavities of the fetus was observed. In the 22nd week of pregnancy it was decided to perform again the thoracocentesis and cordocentesis. The fetal blood cell count and biochemical parameters were normal excluding decreased level of total serum protein (2.54 g/dl) and albumin (2.03 g/dl). Therefore, human albumin solution was injected to the umbilical vein. Afterwards fast regression of hydrothorax was observed. During next two weeks slow increase in pleural effusion was observed together with slight ascites and skin edema. Thus the cordocentesis was performed again in 24th week of pregnancy (fetal blood parameters similar to the previous ones) and human albumin solution was injected. The therapy was performed again in 26th, 28th and 30th week of pregnancy due to increasing symptoms of NHF. Interim improvement was achieved. In 30th week of pregnancy preterm premature rupture of membranes was diagnosed but the range of amniotic fluid index (AFI) according to Phelan stayed within normal limits. Inflammation markers were negative (leucocytosis, acute-phase proteins, cervical culture, body temperature), yet antibiotic was administered as prophylaxis. Due to re-increase of pleural effusion, preterm premature rupture of membranes and the risk of ascending chorioamnionitis, a caesarian section was performed in 32nd week of pregnancy (Velemínský & Tosner, 2008). Just before the cesarean section a decompressing thoracocentesis was performed, so the neonatologists could provide effective ventilation of the fetal lungs after the delivery. A premature newborn male of 2890g was delivered by the cesarean section and obtained 4 points of Apgar score. The intensification of hydrops was well reflected in the neonate high birth weight. The neonate survived, however additional postnatal diagnostic procedures did not reveal the cause of hydrops fetalis.

Second case

A 28-year old woman in her second pregnancy (after miscarriage in previous pregnancy) was admitted to the hospital in 18th week of pregnancy because of fluid accumulation in the subcutaneous tissue of the fetal head and thorax. Moreover, using the ultrasound the following were diagnosed: a small amount of fluid in the fetal peritoneal cavity, placenta of normal thickness, normal amount of amniotic fluid and no congenital malformations of the fetus. Genetic amniocentesis showed normal female karyotype. Maternal blood tests did not reveal any abnormalities. In 20th week of pregnancy it was decided to perform cordocentesis. The fetal blood cell count and biochemical parameters were correct excluding a decreased level of total serum protein (2.2 g/dl) and albumin (1.95 g/dl). Therefore human albumin solution was injected to the umbilical vein resulting in edema decrease. During next two weeks slow accumulation of fluid in subcutaneous tissue, peritoneum and pleural cavities of the fetus was observed. Therefore cordocentesis was performed again in 24th week of pregnancy. Fetal blood parameters were similar to the previous ones and human albumin solution was again injected to the umbilical vein. The therapy was implemented in 26th, 28th and 30th week of pregnancy due to increasing edema and each time resulted in periodic recovery. In 31st week of pregnancy cardiotocographic records and the umbilical artery and middle cerebral artery Doppler indices revealed signs of fetal distress. A premature newborn female of 2750g was delivered by a cesarean section and obtained 6 points of Apgar score. The neonate survived but the cause of NHF remained unknown.

DISCUSSION

NHF occurs in 1:2500 to 1:3500 pregnancies (Faure *et al.* 2004). Ultrasound markers of this condition are: skin edema (fluid layer up to 5 mm wide, usually accumulated in the area of head and neck), pleural effusion, pericardial effusion (over 2 mm), ascites, placental edema (placenta over 5 cm thick), abnormal amount of amniotic fluid (usually polyhydroamnios, in some cases oligohydramnios) (Merz, 2004).

The initial stage of NHF may differ. In our first case the initial sign of NHF was pleural effusion whereas in the second one skin edema appeared. Not all the symp-

toms of NHF listed above must appear, e.g. in both our cases placental edema and changes in the amount of amniotic fluid were not observed.

There are many pathophysiologic events resulting in abnormal accumulation of fluid in fetal compartments. Their recognition is of vital significance to differential diagnosis. The most frequent cause is the increased venous pressure as a result of failure of the cardiovascular system which is caused by different conditions (structural malformations, cardiac arrhythmia, serious anaemia, myocarditis) (Abrams *et al.* 2007; D'Amelio *et al.* 2006; Rose *et al.* 2005; Zeltser *et al.* 2003). The other cause is the decrease of the oncotic pressure resulting from lowered synthesis or an increased loss of proteins (congenital malformations, kidney and liver diseases) (Rodriguez *et al.* 2005; Ismail *et al.* 2001). The decreased level of proteins in the fetal blood may be the primary or secondary symptom of NHF, however it appears in most fetuses with NHF as a result of a chronic oxygen deficiency causing an increase in the permeability of vessels.

NHF etiology is heterogeneous and many factors may influence the final effect which is fetal hydrops. The number of factors to be considered makes the diagnosis complex and difficult. Nevertheless, the diagnostic process should never be abandoned as only the causal treatment may ensure long-lasting therapeutic effects. Despite many efforts, in 40% of cases it is impossible to identify the cause of NHF, as it was indicated in the cases described above (Merz, 2004). In such case the management consists in symptomatic therapy, fetal monitoring and a preterm delivery.

The mortality of neonates with NHF is high and varies from 60 to 81% (Abrams *et al.* 2007; Isaacs, 2008). In the cases described above our management resulted in the survival of the neonates.

Conclusions

Multidirectional diagnostic approach is essential for the implementation of causal treatment of NHF.

In case of idiopathic NHF the only management is symptomatic therapy, fetal monitoring and preterm delivery.

REFERENCES

1 Abrams ME, Meredith KS, Kinnard P, Clark RH (2007). Hydrops fetalis: a retrospective review of cases reported to a large national database and identification of risk factors associated with death. Pediatrics. **120**: 84-89.

2 Czuba B, Borkowski D, Cnota W, Sieroszewski P, Grettka K, Pietryga M, et al (2007). Ultrasonographic assessment of fetal nuchal translucency (NT) at 11th and 14th week of gestation-Polish multicentre study. Neuro Endocrinol Lett. **28**: 175-181.

3 D'Amelio R, Rauccio V, Melluso J, Dettori C, Grande S, Feraudo E, et al (2006). Non-immune fetal hydrops: a case report. Clin Exp Obstet Gynecol. **33**: 241-243.

4 Faure R, Dreux S, Dommergues M, Dumek Y, Luton D, Oury JF, et al (2004). Nonimmune fetal ascites: a series of 79 cases. Am J Obstet Gynecol. **190**: 407-412.

5 Isaacs H (2008). Fetal hydrops associated with tumors. Am J Perinatol. **25**: 43-68.

6 Ismail KM, Martin WL, Ghosh S, Whittle MJ, Kilby MD (2001). Etiology and outcome of hydrops fetalis. J Matern Fetal Med. **10**: 175-181.

7 Merz E, editor (2004). Diagnostyka ultrasonograficzna w ginekologii i położnictwie. [(Ultrasound in obstetrics and gynecology) (In Polish)] Wrocław: Urban & Partner.

8 Rodriguez MM, Bruce JH, Jimenez XZ, Romaguera RL, Bancalari E, Garcia OL, et al (2005). Nonimmune hydrops fetalis in the liveborn: series of 32 autopsies. Pediatr Dev Pathol. **8**: 369-378.

9 Rose CH, Bofill JA, Le M, Martin RW (2005). Non-immune hydrops fetalis: prenatal diagnosis and perinatal outcomes. J Miss State Med Assoc. **46**: 99-102.

10 Velemínský M, Tosner J (2008). Relationship of vaginal microflora to PROM, pPROM and the risk of early-onset neonatal sepsis. Neuro Endocrinol Lett. **29**: 205-221.

11 Zeltser I, Parness IA, Ko H, Holzman IR, Kamenir SA (2003). Midaortic syndrome in the fetus and premature newborn: a new etiology of nonimmune hydrops fetalis and reversible fetal cardiomyopathy. Pediatrics. **111**: 1437-1442.