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A Case Report of Complete Resolution of Nonimmunological Hydrops Fetalis Without Known Etiology

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ABSTRACT

The prevalence of nonimmunological hydrops fetalis has been reported between 1 in 1500 and 1 in 4000, with an approximate 80% mortality rate. This case-report study explains a case of hydrops fetalis, presented with generalized edema and pleural and pericardial effusion at 30 weeks of gestation with preterm birth at this age due to preterm uterine contractions. No etiology was found for hydrops and all signs resolved thoroughly after birth without treatment. After birth, the newborn was admitted to neonatal intensive care unit and discharged after 47 days in good condition. The infant was completely healthy within three months after delivery.

Keywords: Complete resolution, idiopathic, Hydrops fetalis, Spontaneous resolution, Non-immunological

Introduction

Hydrops fetalis means the abnormal collection of fluid in fetal soft tissues and serous cavities. Nonimmune hydrops fetalis (NIHF) includes cases not affected by red cell alloimmunization. The incidence of NIHF is 1:1500 to 1:4000. At the moment, NIHF includes about 90% of hydrops fetalis cases **(1-2)**.

The prenatal diagnosis of hydrops fetalis is based on ultrasound examination findings, including two or more of the following: ascites, pleural effusion, pericardial effusion, Skin edema (>5 mm). The etiology is determined in 60% to 85% of cases, prenatally or postnatally **(3)**. The etiology of hydrops cases is related to the gestational age of presentation. NIHF before 24 weeks of gestation is usually related to an aneuploidy, whereas cardiac and pulmonary anomalies, and infectious disease cause most cases after 24 weeks of gestation **(4)**. Cardiovascular abnormalities are reported in 40% of cases of NIHF **(5)**. Aneuploidy is responsible for seven to 16% of NIHF cases. The most common aneuploidy associated with NIHF is monosomy X (5). Severe fetal anemia due to high output cardiac failure **(6)** accounts for 10% to 27% of cases **(5)**. Infections are responsible for five to 10% percent of NIHF cases **(7)**. Parvovirus B19 is the most common infection in hydropic fetuses. Thoracic anomalies account for 10% of the cases. Primary congenital pulmonary lymphangiectasis results from thoracic duct obstruction, while secondary congenital pulmonary lymphangiectasis results from thoracic masses or congenital heart disease **(8-9)**. Fetal/placental vascular tumors due to arteriovenous shunting and high cardiac output failure can lead to hydrops. Metabolic disorders include a group of autosomal recessive diseases present in the fetal period as NIHF **(7)**. Skeletal dysplasias may be the cause of nonimmune hydrops fetalis **(7)**.

NIHF is associated with a perinatal mortality rate of 50% to 98% **(10-12)**. Prognosis depends on the etiology, the gestational age at the onset of hydrops, the gestational age at delivery, and the presence of pleural effusions. Generally, the early hydrops is associated with poorer outcome. Pleural effusions and

polyhydramnios before 20 weeks of gestation due to increased risks of pulmonary hypoplasia and preterm delivery are poor prognostic factors. The absence of aneuploidy and major structural anomalies have a better outcome **(13)**.

The present report explains a case of hydrops fetalis with unknown etiology and complete resolution after birth.

Case Presentation

A 31 years old gravid2 woman with a previous cesarean delivery was referred to Yas hospital at 30 weeks of gestation. The chief complaint was labor pain, and the patient had an ultrasound report of polyhydramnios (AF=38) that had been performed about two weeks ago. Our center's ultrasonographic examination showed severe hydrops fetalis with generalized edema, bilateral hydrothorax and collapsed lungs, and pericardial effusion (see Figures 1-7). The amniotic fluid index was 45cm; neither anemia nor fetal anomaly was detected. Biometric parameters were appropriate for the gestational week. A detailed ultrasound examination for anomalies of the fetus, placenta, and the umbilical cord was done before delivery by a maternal-fetal specialist, and no abnormal finding was found. An overview of maternal documents and the first and second-trimester aneuploidy screening was indicative of low risk. Nucal thickness in the first trimester was in the normal range; detailed ultrasound examination for anomaly scanning at 20 weeks of gestation was normal. Due to the rapid progression of labor to the active phase, the cesarean section was done in the presence of a neonatologist, and a female infant weighing 1800 g, with Apgar 3 and normal ABG, was delivered. Intubation was done, and the newborn was admitted to neonatal intensive care unit (NICU). Further evaluation to detect the cause of hydrops fetalis was done after delivery.

After birth, in neonatal evaluation, a detailed examination of the newborn was done by a neonatologist, and there was no abnormal finding. Polymerase chain reaction (PCR) test for toxoplasma, rubella, parvovirus B19 of blood specimens, and PCR test for cytomegalovirus (CMV) on urine specimen were negative. As congenital cardiac diseases are one of the most well-known causes of NIHF, we performed neonatal echocardiography after birth, and it was normal (we did not have enough time to do it before delivery). Fetal heart rate (FHR) pattern before birth was regular. The middle cerebral artery Doppler studies to assess fetal anemia and newborn hemoglobin were in the normal range (14.9); therefore, anemia was not considered.

The umbilical cord and placenta appeared normal and histopathologic examination by a pathologist showed no abnormality.

In maternal evaluation, complete blood cell count and indices were normal. The maternal blood group was A+, the antibody screen was negative, serologic test for syphilis, and antibodies for toxoplasma, CMV, rubella, and parvovirus B19 were negative.

Genetic abnormalities as a cause of NIHF must be excluded. Familial history to rule out an inherited disorder in the family is essential. In our case, family history was negative, and karyotype evaluation after birth showed a normal female chromosomal complement, and no further evaluation was done. The analysis of thoracentesis fluid was normal with negative culture. In the end, we did not find any abnormal findings.

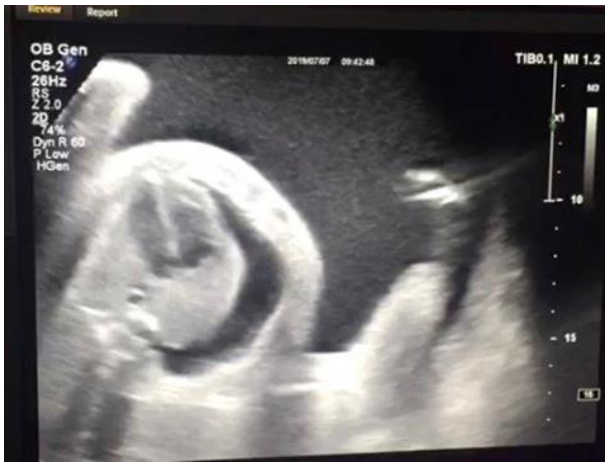

Figure 1. Bilateral pleural effusion in Transverse view of the fetal thorax

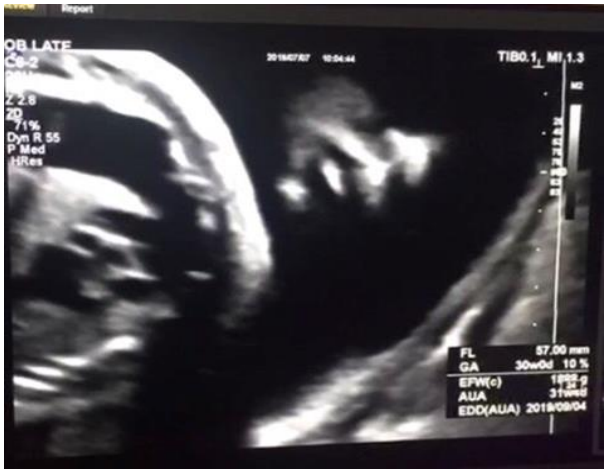

Figure 2. Coronal view of the face with normal lip and mouth

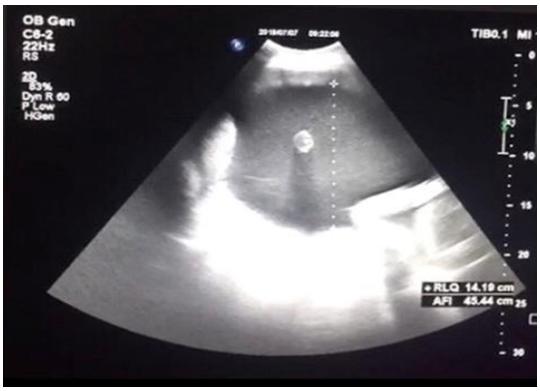

Figure 3. **Maximal vertical pocket**

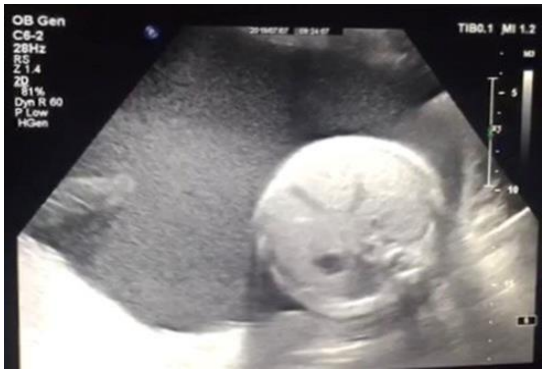

Figure 4. **Transverse view of the fetal abdomen without ascites**

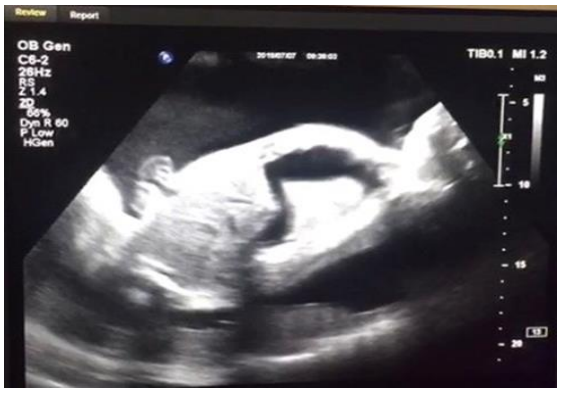

Figure 5. **Sagittal view of the fetus with severe pleural effusion**

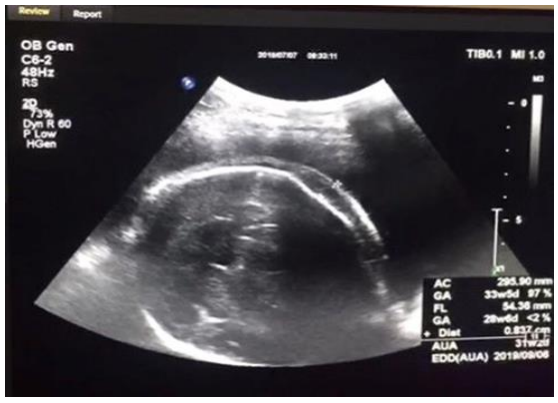

Figure 6. **Fetal skull with skin edema**

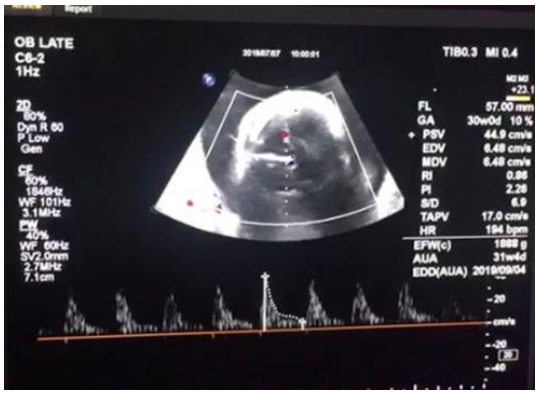

Figure 7. **The middle cerebral artery Doppler**

The newborn was admitted to NICU and thoracentesis was done (20 cc). Ventilatory support and surfactant replacement were carried out to treat respiratory distress syndrome (RDS), similar to other premature infants. The infant was discharged after 48 days in good condition. The child was entirely healthy, physical and neurodevelopmental status was normal till 6 months after delivery.

Discussion

Sonographic diagnosis of hydrops fetalis is simple. The issue is to determine the etiology, the proper therapy, timing of delivery, and evaluation of prognostic factors.

Few cases of idiopathic hydrops fetalis with total resolution have been reported in the literature. Iskaros reported 45 cases of nonimmunological fetal hydrops between 11 and 17 weeks of gestation during four years. Four of these cases were considered as idiopathic cases, and in all of them, the hydrops resolved before 24 weeks of gestation **(14)**.

Ramon *et al.* examined prognostic factors in NIHF. Ultrasonographic evidence of malformation and/or the presence of persistent pleural effusions were two factors associated with poor perinatal outcome. When pleural effusions were demonstrated by ultrasound and lung, the thoracic ratio was less than 0.6, severe lung hypoplasia was documented by histopathologic examination, and the perinatal mortality rate was 100% **(15)**. Therefore the absence of these two factors is associated with a better outcome, which is in accordance with our case.

A retrospective cohort study was conducted by Nassr *et al.*, including 142 cases of NIHF. They evaluated the effect of etiology, location of fluid collection, and gestational age at delivery on survival. According to underlying etiology, nonimmune hydrops was associated with a 37% risk of neonatal mortality and a 50% chance of survival. Ascites independently predicted perinatal mortality **(16)**. In our case, we did not find ascites that can be compatible with a good prognosis before and after birth.

KIM, Lee *et al.* conducted a numeric score called the ultrasonographic severity scoring of non-immune hydrops (USNIH). Perinatal mortality rate was higher in patients with USNIH≥3 points compared to those who scored 2 points. They found this system may be reliable to predict perinatal outcomes in nonimmune hydrops, especially in idiopathic cases **(17)**. According to this article, there are some criteria to predict the prognosis of NIHF that can guide us in managing these cases.

Swain *et al.* surveyed the prevalence, etiology, and outcome of 40 cases of nonimmunological hydrops fetalis. Only two of the 14 idiopathic cases survived. The first one was diagnosed at 31 weeks of gestation, and the second case at 30 weeks of gestation **(18)**. This shows the importance of the gestational age at which hydrops fetalis is diagnosed. Like the two cases mentioned in this study, our case has a late onset of hydrops fetalis.

In the present case-report, we described a fetus with nonimmunologic hydrops fetalis, which had unknown etiology, and resolved entirely with no intervention after preterm birth. We conclude that even severe nonimmunologic hydrops fetalis can resolve completely, especially if there are no associated congenital malformations, chromosomal disorders, intrauterine infections, or tumors, and particularly when it is diagnosed late in pregnancy, similar to our case. Due to the probability of spontaneous resolution and good outcome in these rare cases with an idiopathic etiology, conservative expectant management should be the first treatment choice.

In our case, we did not expect a good prognosis according to ultrasound findings that were compatible with severe hydrops fetalis. Pleural effusion was massive, and the lungs appeared hypoplastic. A straightforward attitude to this case, considering no signs of associated congenital malformations, late onset of the disorder, and negative familial history, could favor a good prognosis. These early findings could give us a choice to select a more conservative approach, including inhibition of uterine contraction with tocolysis, amnioreduction for maternal comfort and resolving uterine distention, and maybe intra uterine interventions like the placement of a thoracic shunt. Xia *et al.* examined twelve cases with severe fetal primary hydrothorax, who underwent prenatal intervention. They concluded antenatal intervention might enhance the chance of survival in severe primary fetal hydrothorax **(19)**.

Conclusion

According to this case report and other mentioned studies, severe NIHF is not necessarily associated with poor prognosis, and conservative management should be considered.

Acknowledgments

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Conflict of Interest

There authors have no conflict of interest.

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