

PRENATAL INVESTIGATION AND MANAGEMENT OF NON-IMMUNE HYDROPS FETALIS

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Abstract: Background: Advances in medicine have significantly improved our ability to address various diseases affecting the unborn child, with fetal medicine emerging as a rapidly evolving field. **Specific Background:** Nonimmune hydrops fetalis, a severe antenatal pathology requiring advanced minimally invasive treatment techniques, exemplifies the critical challenges and progress in fetal medicine. **Knowledge Gap:** Despite advancements, there remains a need for a comprehensive review of nonimmune hydrops fetalis, encompassing its etiology, clinical presentation, and management, particularly with regard to recent data from specialized fetal medicine departments. **Aims:** This article aims to review the multifaceted aspects of nonimmune hydrops fetalis, including its causes, diagnostic approaches, and treatment options, while providing insights from recent cases managed within a fetal medicine department. **Results:** The review covers the etiology of nonimmune hydrops fetalis, which can be attributed to a range of genetic, cardiac, and infectious factors. It discusses the clinical presentation and highlights advancements in antenatal diagnosis and management. Additionally, the article presents case studies from the fetal medicine department, illustrating contemporary approaches and outcomes. **Novelty:** This review provides an updated synthesis of nonimmune hydrops fetalis management and diagnosis, integrating recent case studies and technological advancements. **Implications:** The findings underscore the importance of continued research and innovation in fetal medicine to enhance the diagnosis and management of nonimmune hydrops fetalis, ultimately improving outcomes for affected pregnancies.

Keywords: Non-Immune Hydrops Fetalis, Paracentesis, Thoracocentesis, Cordocentesis, Amnioreduction



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Introduction

Hydrops fetalis is one of the serious pathologies characterized by high mortality in both the antenatal and postnatal periods. Hydrops fetalis is the last stage for a number of intrauterine diseases. The prevalence of hydrops is 1 in 1000-14000 births. Usually, no more than 20-30% of newborns survive with this diagnosis. The survival rate of infants with this pathology, according to various sources, ranges from 27 to 36% [9,11]. Hydrops fetalis, according to the ICD X revision, is subdivided into: 1) Hydrops fetalis caused by hemolytic disease (immune hydrops - P56) and 2) Hydrops fetalis not associated with hemolytic disease (non-immune hydrops - P83.2). The distinction between immune and non-immune hydrops was first identified in 1943 by Edith Potter. At that time, non-

immune hydrops was rare and accounted for less than a quarter of children born with hydrops [3,5,10]. Nowadays, given the widespread use of Rh sensitization prophylaxis, non-immune hydrops fetalis (NF) has become the predominant form among all types of hydrops fetalis. Among all cases of hydrops fetalis, non-immune hydrops fetalis (NF) occurs up to 90% [5,9]. Its frequency, according to large-scale studies, ranges between 1: 2000-1: 3000 pregnant women [4,5].

Non-immune hydrops fetalis is a polyetiological pathology described by pronounced signs of general hydration due to the accumulation of extracellular fluid in the serous cavities and tissues of the fetus in the absence of signs of isoimmunization [1–3]. On ultrasound, the typical symptoms of non-immune hydrops fetalis are: generalized subcutaneous edema (> 5 mm at the level of the skull or chest), hydrothorax, ascites, and pericardial edema. The diagnosis is confirmed by the detection of fluid accumulation in more than one serous cavity of the fetal body. This feature distinguishes non-immune fetal hydrops from isolated hydrothorax, ascites, pericardial edema, cystic hygroma, or occipital edema [7,9].

The etiology of non-immune hydrops fetalis is very diverse. In the early stages of pregnancy, NIHF develops mainly due to chromosomal abnormalities, and in other cases, the causes may be pathologies of the cardiovascular system, lymphatic system, syndromic pathologies, infections, FTTS, urinary tract anomalies and many others [6,11,12].

The etiology of non-immune hydrops fetalis is a decisive factor in the choice of pregnancy management tactics and intrauterine treatment options. According to the Canadian Society of Obstetricians and Gynecologists (SOGC), with a normal fetal karyotype, a gestational age of more than 18 weeks, fetal therapy and / or surgical interventions lead to positive results [1,3,8,12]. The type of intrauterine intervention is determined depending on the etiology, clinical manifestations and concomitant pathology of NIHF.

Methods

20 patients with a diagnosis of NIHF with a normal karyotype, who were treated at the Republican Specialized Scientific and Practical Medical Center of Obstetrics and Gynecology, were examined. Patients underwent Doppler ultrasound, PCR and IFA studies for infections, diagnostic and therapeutic cordocentesis, amniocentesis, amnioreduction, paracentesis, thoracocentesis and conservative treatment.

All patients participating in the study underwent an ultrasound examination and assessed the following parameters: the presence of structural pathology in the fetus, the number of fluid-filled serous cavities, the volume of fluid collected, the presence and degree of pulmonary hypoplasia, cardiac compression, soft tissue edema, thickness, spread and the amount of amniotic fluid and the thickness of the placenta. On the Doppler study, attention was paid to the peak systolic blood flow velocity in the middle cerebral artery, which is a sign of severe anemia above 1.5 MOM. After 20 weeks of gestation, fetal echocardiography was performed to assess functional and structural pathologies of the heart, valves and magistral vessels, the presence and volume of fluid in the pericardial cavity and a number of parameters indicating the functional state of the heart.

From the moment of hospitalization of the pregnant woman to the hospital until the moment of delivery, the condition of the fetus was regularly monitored using ultrasound, dopplerometry and cardiotocography.

Results and Discussion

Results

Of the 20 examined patients, 19 were singletons. The age of the woman is from 19 to 38 years. The median gestational age for which non-immune hydrops fetalis was first detected on ultrasound was 27 weeks, with a lower and upper limit of 21–34 weeks.

Of the 20 examined patients with non-immune hydrops fetalis, 9 patients were found to have an infection. HSV was detected in 4 cases, CMV - in 1 patient, HSV+CMV - in 2 patients, SARS-CoV-2 - in 2 cases. Heart pathology was noted in 4 cases, in all patients occurred tachyarrhythmia. Congenital cystic adenomatoid malformation (CCAM) was detected in 1 patients. In 1 patients, as a result of FTTS, non-immune hydrops fetalis was developed. Chorionangioma occurred in 1 patient. In 1 case was noted anomalies of urinary tract, in 1 patient syndromal pathology, in 1 patient genetic disorders. And in other 1 patient was detected congenital peritonitis of fetus.

Treatment of non-immune hydrops fetalis includes etiotropic treatment aimed at eliminating the underlying etiology of the disease, and symptomatic treatment aimed at relieving symptoms, reducing complications and prolonging pregnancy.

Etiotropic treatment includes antiarrhythmic drugs used for fetal arrhythmias, cardiac glycosides used for heart failure, intrauterine blood transfusion for fetal anemia, surgical correction of fetofetal transfusion syndrome.

Measures to eliminate ascites and hydrothorax include multiple centesis or shunting procedures to help drain fluid from the serous cavities. The literature describes cases of installing a thoracoamniotic shunt at 22 weeks of gestation, which made it possible to prolong the pregnancy.

In cases where permanent shunting is not possible, thoracocentesis or paracentesis is performed to prevent pulmonary dysplasia. In cases where polyhydramnios is involved, amnioreduction is the method of choice.

The expediency of the practice is decided at a consultation with the participation of an obstetrician-gynecologist, an ultrasound diagnostician, a geneticist, and a pediatric surgeon.

In our study, paracentesis was performed in 5 patients, in 1 patient the operation was repeated 5 times. In all cases, almost complete evacuation of the liquid was achieved. The volume of the extracted liquid ranged from 50 ml to 500 ml. There were no cases of accumulation of fluid in the abdominal cavity after childbirth, repeated paracentesis was not performed.

Of the 20 patients, thoracocentesis was performed in 2 patients and in both patients the operation was successful.

Amnioreduction was performed in 9 patients with polyhydramnios. Conservative treatment was carried out in 17 patients, depending on the etiology. Of these, 4 patients received antiarrhythmic therapy and 11 fetuses with symptoms of heart failure received treatment with cardiac glycosides. Immunoglobulin therapy was carried out in 9 patients who developed non-immune hydrops fetalis against the background of infection, and in 14 cases the treatment was completed successfully, the symptoms of non-immune hydrops fetalis were eliminated, the children were born healthy.

Of the 20 patients, 9 had term delivery, 11 had preterm birth, 3 had antenatal fetal death, and 1 had late neonatal mortality. The number of surviving children consisted 14.

As for the algorithm for managing pregnancy in non-immune hydrops fetalis, it is based on the identification of an etiological factor. If non-immune hydrops fetalis are detected in the early stages of pregnancy, the pregnant woman should be informed about the condition of the fetus and its adverse consequences, especially when chromosomal pathology is detected, the possibility of abortion for medical reasons.

With cordocentesis, the hematocrit and the amount of hemoglobin in the fetal blood are determined. In addition, fetal blood is analyzed for the presence of proinflammatory mediators,

procalcitonin, IL-6, C reactive protein and TORCH infections. Anemia is an indication for intrauterine blood transfusion.

With a normal karyotype, when no signs of an acute infection are detected, and with a normal blood composition, dynamic monitoring is carried out. When persistent or increasing fetal hydrothorax or ascites is observed, as well as in cases where conservative treatment is ineffective, thoracocentesis and / or fetal paracentesis are used to prevent the development of severe pulmonary hypoplasia and other complications. Fluids from the serous cavity are examined for the presence of inflammatory mediators and TORCH infection. In cases of polyhydramnios, amnioreduction and fluid analysis are performed.

Conclusion

With the development of methods for the prevention and treatment of immune hydrops of the fetus with Rh-sensitization, the prevalence of non-immune hydrops of the fetus is increasing. Although the vital prognosis of the fetus is unfavorable, the algorithm developed by us for managing pregnancy with non-immune fetal hydrops allows us to timely assess the prognosis for the fetus and determine the possibilities and tactics of etiotropic and symptomatic treatment. Early diagnosis of non-immune fetal dropsy is of great importance, as it allows to identify the etiological factor as soon as possible after diagnosis, which expands the possibilities of treatment.

Ultrasound is the most optimal diagnostic tool for antenatal diagnosis of non-immune fetal hydrops with all Doppler studies. Of great importance for the diagnosis of the disease are a detailed anamnestic history and examination of the mother. In addition, serological testing for perinatal infections in the fetus and maternal antibodies may help determine the etiology of non-immune fetal hydrops. For children who have not received antenatal diagnosis and treatment, the outcome is considered very dangerous and unfavorable, with an increase in perinatal morbidity and mortality.

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