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CASE REPORT / OLGU SUNUMU

Non immune hydrops fetalis: Two premature infants with favorable outcome

Non immun hidrops fetalis: İyi prognozlu iki prematüre olgu

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ABSTRACT

Non immune hydrops fetalis is defined as the excessive accumulation of fluid in two or more compartments of the fetus in the absence of any maternal-fetal blood incompatibility. The clinical presentations include ascites, scalp edema, pleural or pericardial effusions and polyhydramnios. Perinatal mortality in this severe clinical condition is high, between 50-98%. Prematurity is an important risk factor for mortality. Despite many advances in diagnosis, therapy and ventilation management during the last decade in neonatal intensive care units, the mortality rate has not changed very much for hydropic infants. This is the report of the management of two premature infants born severely hydropic. The first infant had tachyarrhythmia, the second infant had Noonan syndrome. Both infants had a good prognosis.

Key words: Non immune hydrops fetalis, Fetal tachyarrhythmia, Noonan syndrome

ÖZET

Non immun hidrops fetalis anne ve bebek arasında kan uyuşmazlığı olmaksızın fetüsde iki veya daha fazla vücut boşluğunda fazla sıvı birikmesi olarak tanımlanır. Asit, saçlı deride ödem, plevral ve perikardiyal efüzyon ve polihidramnios klinik tabloyu oluşturur. Bu ağır klinik tabloda perinatal mortalite %50-98 arasında yüksektir. Prematüre doğum mortalite için önemli bir risk faktörüdür. Yenidoğan yoğun bakım ünitelerinde son on yılda tanı, tedavi ve ventilasyon uygulamalarındaki gelişmelere rağmen, hidropik bebeklerde mortalite oranları fazla değişmemiştir. Bu yazıda hidropik doğan iki prematüre bebeğin takibi sunulmuştur. Birinci olguda fetal taşiaritmiye, ikinci olguda Noonan sendromuna bağlı non immun hidrops fetalis gelişmiştir. İki vakada da prognoz iyi olmuştur.

Anahtar kelimeler: Non immun hidrops fetalis, Fetal taşiaritmi, Noonan sendromu

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Introduction

Hydrops fetalis (HF) is defined as the excessive accumulation of fluid in two or more interstitial compartment of the fetus. The presentations are ascites, scalp edema, pleural effusions, pericardial effusions leading to anasarca and polyhydramnios [1]. These clinical findings with the absence of maternal-fetal blood incompatibility define non immune hydrops fetalis (NIHF). The widespread use of Rh(D) immnunoglobulin has dramatically decreased the prevalence of Rh isoimmunisation and NIHF accounts for almost 90% of hydrops cases currently [2].

The incidence of NIHF varies from 1 in 830 to 1 in 3500 deliveries [3]. About 10 to 20% of cases are idiopathic. The most common conditions associated with NIHF are congenital heart defects and rhythm abnormalities (19-25%), chromosomal disorders (35%), infections (1-8%) and some other syndromes (9%) [3]. The commonest chromosomal anomaly is Turner syndrome. Genetic syndromes such as achondrogenesis types 1B, and 2, arthrogryposis multiplex congenita, Cornelia de Lange, myotonic dystrophy, Noonan syndrome (NS), Prune belly, tuberous sclerosis, and inborn errors of metabolism such as glycogen storage disease type 4, lysosomal storage diseases, carnitine deficiency, and thyroid disease have all been described as associated with NIHF [1].

This article includes two hydropic premature infants with favorable outcome.

Case Reports

Case 1

The mother, a 28 year-old primigravida, noticed the sudden cessation of fetal movements at the 31st week of an uneventful pregnancy. Ultrasonographic examination confirmed the diagnosis of fetal tachycardia and hydrops fetalis. The hydropic male infant was delivered by an emergency cesarean section. The birth weight was 2300 g, and the apgar scores were 1/4/5 at 1, 5 and 10 min respectively. He was resuscitated and surfactant was administered in the delivery room. Generalised massive skin and scalp edema and ascites were present on physical examination. He needed

high pressure ventilation with a peak inspiratory pressure of 34 cmH_2O and a positive end expiratory pressure of 7 cmH_2O and FiO_2 100% during the first hours of life. Massive ascites and a minimal pleural effusion were detected by ultrasound. Edema was treated with 10% human albumine infusion (1gr/kg during two hours) followed by furosemide (1 mg/kg/dose IV) and paracentesis was performed. After the second dose of surfactant therapy at the third hour of extrauterine life the ventilation parameters were decreased gradually. Cranial ultrasonography revealed hyperechogenic areas due to edema. Electrocardiograpy (ECG) showed a Wolff-Parkinson-White (WPW) pattern while echocardiography (ECHO) was normal. Mechanical ventilation was needed for two days and the patient's weight dropped to 1890 g on the third day.

The patient had recurrent paroxysms of tachycardia (300/min), with good response to adenosine on his fifth day of life. Consequently the patient was treated with oral digoxine (6 µg/kg/day) and propranolol (2 mg/kg/day). Further recovery was uneventful and he was discharged on day 21.

Since tachyarrhythmia did not repeat, the medication was discontinued at one-year of age. The neuro-motor development was normal at two year of age.

Case 2

A small pleural effusion and nuchal thickness in the fetus was detected at the routine examination of a 42 year old gravida 2, para 1 mother at the 18th week' of gestation. Pleural effusion was resolved spontaneously in a month. Amniocentesis was performed because of the increased fetal nuchal thickness and revealed a normal karyotype. However a mutation in the PTPN11 gene was found. The fetal ECHO was normal. Pleural effusion bilaterally was detected at 31+3 gestational weeks and progressed to hydrops fetalis during 48 hours. The mother was referred to our hospital for the delivery of this high risk baby. The delivery was performed by C/S and the apgar scores were 5/7/8 at 1, 5 and 10 min respectively. Birth weight was 2500 g. The baby had ascites and severe generalized edema. She was intubated in the delivery room, given surfactant and bilateral thorax drainage was performed just after the delivery.

The total thorax drainage was 340 ml during the first hour after delivery and microscopic investigation revealed 90% lymphocytes with sterile culture, which is compatible with chylothorax. Structural anomalies of the heart were ruled out by ECHO at the first day of extrauterine life. The weight dropped to 1850 g on the third day. Since the chylothorax persisted (120 ml/day) despite total parenteral nutrition and minimal enteral feeding with a medium chain triglyceride (MCT) formula, intravenous octreotide infusion was started (5µg/kg/h) on day 7. The chylothorax was then managed successfully. There were no side effects related to the octreotide therapy. The baby was extubated on day 11. A second ECHO performed because of a murmur on day 15 revealed pulmonary valve stenosis. Total parenteral nutrition was stopped on day 19 and the MCT formula was transitioned to breast milk on day 30. Hypertelorism and epicanthic folds were prominent when the baby was 1 month old. She was discharged home at 39th day of life.

The PTPN11 mutation is commonly found in NS. The pulmonary stenosis, hypertelorism and epicanthic folds in this baby are clinical features of NS. The first ECHO performed after delivery was normal as cardiac anomalies in NS are late-onset progressive pathologies. The second echocardiographic examination was performed because of a newly heard murmur and revealed mild pulmonary valve stenosis. Any intervention for the the pulmonary stenosis was not needed in the first year of life. The neurodevelopmental assessment at one year of age was normal.

Discussion

Non-immune hydrops fetalis presenting before 24 weeks is usually due to chromosomal aberrations, while hydrops presenting after 24 weeks's gestation is usually due to structural anomalies [2]. In accordance with this, first fetus with the WPW syndrome developed hydrops after 30th week's of gestation. However, the pleural effusion was detected at the 18th week of gestation in the second fetus with the PTPN11 mutation. Lymphatic vessel dysplasia, hypoplasia, or aplasia are common findings in NS (20%) and this disorder of lymphatic development may cause peripheral lymphedema, chylothorax, and NIHF [4]. Thus pleural effusion may be the early presentation of NIHF.

Heart rhythm disorders are a common cause of NIHF. The incidence of NIHF in fetal supraventricular tachycardia is between 35-60% [5,6]. The physiologic volume overload of the fetal right heart and the reduced compliance of the fetal ventricular myocardium increases the risk of the fetus developing systemic edema. Impaired protein synthesis due to passive congestion of the liver may precipitate rapid development of fetal NIHF [5]. The treatment of fetal arrhythmias is possible by administration of medications to the mother. Digoxin is the first-choice drug for the treatment of in utero fetal tachyarrhytmias. In the event of sustained fetal tachycardia despite maternal administration of digoxin, β blocking agents are the second agent generally used and flecainide can be considered as a third-line therapy [5,6]. Close monitoring of the mother's heart is essential when medication is done.

Because of the low umbilical cord blood flow in Doppler ultrasound, medical management was not possible in the first case with in utero fetal tacharrhythmia and delivery was done by emergency c/s. However, the hydropic fetus and placenta tend to absorb maternally administered antiarrhythmic agents less well than the nonhydropic fetuses [5].

Needle aspiration of pleural effusions, feto-amniotic shunting and amnioreduction are usual antenatal surgical interventions in hydrops fetalis. These interventions are

associated with a high risk of preterm premature rupture of membranes or chorioamnionitis and may provoke preterm labor. Thoracentesis before delivery may facilitate neonatal resuscitation in some cases [7].

There are no evidence-based guidelines about the best time and mode of delivery for hydropic babies. Since prematurity is an important risk factor for mortality in NIHF, delivering fetuses early to treat worsening hydrops may not improve survival rates. However intrauterine death is another risk. Delivery is recommended if fetal testing becomes non-reassuring, if pre-eclampsia complicates the hydrops or preterm labour is established. Cesarean section has not been shown to improve neonatal outcome, but it does allow for a planned resuscitation by the neonatal team and may avoid the problem of soft tissue dystocia [7].

Hydrops fetalis may result in intrauterine or early postnatal death, sometimes even in the delivery room [1]. Both infants were born by C/S and the neonatal intensive care team were informed about the condition and history of the babies before delivery in detail. Two doctors experienced in preterm resuscitation were ready in the delivery room in both cases. For the second infant, since the obstetrician emphasized the bilaterally massive pleural effusion, a pediatric surgeon was also ready in the delivery room. While one was intubating the baby other doctors performed thoracentesis bilaterally which enabled ventilation in this case. Early surfactant replacement was needed in both cases in order to achive ventilation. Mechanical ventilation with high peak inspiratory pressure (38 gradually decreased to 30 cmH_2O) during the first hour of life was also needed. Hydrops fetalis is a very severe condition and hydropic babies may need prompt interventions such as intubation and surfactant replacement, umbilical catheterization, thoracentesis or paracentesis in the delivery room. It is important for these deliveries to be done in tertiary-care centers where adequate equipment and an experienced team are available.

The neurodevelopmental outcome of hydropic infants is of concern. The underlying cause of NIHF effects the long-term survival rates. However, 68-90% of survivors have a normal development [8,9]. No neurodevelopmental delay was seen in either infant.

Non immune hydrops fetalis is associated with an overall perinatal mortality rate of 50-98% [10,11]. Mortality rates differ according to the presence of prematurity, chromosomal abnormalities, associated lethal malformations and pulmonary hypoplasia produced by fetal pleural effusions in NIHF. Unexplained cases may have the poorest outcome [1]. Despite many advances in diagnosis and therapy in NICU, the mortality rate has not changed very much over the past 15 years [1,9].

In conclusion, neonatal management of NIHF requires a skilled and coordinated resuscitation team supported by a well equipped neonatal intensive care unit. Preterm infants with NIHF can have good prognosis if structural heart anomalies, chromosomal abnormalities and lethal malformations do not complicate the NIHF.

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