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A case of fetal hydrops: prenatal diagnosis and neonatal management

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Abstract

Hydrops fetalis (HF) is a serious fetal condition defined as an abnormal fluid accumulation in fetal extravascular compartments and body cavities caused by either immune or non immune conditions. Immune hydrops is caused by fetal hemolysis mediated by circulating maternal antibodies to fetal red blood cell antigens. Its most common determinant is rhesus incompatibility. Systemic Lupus Eritematosus (SLE) is another rare cause of immune fetal hydrops, when the pregnancy is complicated by the presence of a third degree congenital heart block (CHB). The Neonatal Lupus Syndrome occurs with a prevalence of 2%.
We reported the case of severe fetal hydrops in a 31 weeks pregnant woman affected by mild maternal D alloimmunization and SLE. Despite fetal hydrops and a mild positive indirect Coombs' test, the flow-rate study with the Systolic Peak Velocity (PSV) of the MCA excluded a fetal anemia. At birth, blood gas showed a condition of severe metabolic and respiratory acidosis (pH 6.43, pO2 9.9 mmHg, pCO2 206 mmHg, Base Excess (BE) -35 mmol/l, HCO3- 2.7 mmol/l) and a mild anemia (Hemoglobin 10.3 g/dl). ECG revealed a normal sinus rhythm and a CHB was excluded. Despite the critical clinical condition, no cardiorespiratory or neurological adverse outcomes occurred in the newborn

Keywords: hydrops fetalis, rhesus incompatibility, Systemic lupus erythematosus

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Introduction

Hydrops fetalis (HF) is a serious fetal condition defined as an abnormal fluid accumulation in fetal extravascular compartments and body cavities leading to edema, ascites, pleural and pericardial effusions, and anasarca (1, 3). It may also be associated with polyhydramnios and placental edema. Its incidence is reported to be 0.3 to 2.4 per 1,000 live births (4, 5). The etiologies are considered as immune or non immune hydrops (6).

Immune hydrops is caused by fetal hemolysis mediated by circulating maternal antibodies to fetal red blood cell antigens (7). Its most common determinant is rhesus incompatibility and it occurs when antibodies from a Rh-negative mother target and destroy 'foreign' red blood cells from a Rh-positive fetus (8). The introduction of postnatal immunoprophylaxis in 1970 reduced the incidence

of maternal D alloimmunization from 14% to 1-2% (9). Post-partum anti-D immunoglobulin administered to Rh D-negative women and routine antenatal anti-D prophylaxis have greatly reduced the incidence of haemolytic disease of the fetus and newborn due to immune anti-D to 0.1% (10) In a Rh-negative mother, maternal anti-D antibodies may cross the placenta and lead to the immune-mediated destruction of fetal red blood cells. This more rapid destruction of the fetal red blood cells than normal can lead to anemia and jaundice and, in very severe cases, kernicterus or even death.

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that mainly affects women of reproductive age. Pregnancies in women with SLE resulted in an increase of adverse pregnancy outcomes (e.g., stillbirth, premature birth, and intrauterine growth restriction) (11). SLE is another rare cause of immune fetal hydrops, when the pregnancy is complicated by the presence of a third degree congenital heart block (CHB). The neonatal lupus syndromes occurs with a prevalence of 2%.

Since there was a decline of rhesus iso-immunization by routine screening and prophylaxis (1, 12), approximately 76-87% of all cases of HF are estimated to be of non-immune origin (6).

Non-immune hydrops can result from a large number of causes including cardiac and non-cardiac anomaly, syndromes, aneuploidy, congenital infection, twin-to-twin transfusion syndrome, chrioangioma and other conditions. Moreover, in 15% to 25% of cases, the precise cause may remain unknown (12,13). Mortality rate is still high, up to 75% (12, 14, 15).

Routine ultrasound examination allows to easily recognize fetal hydrops. A more detailed examination should be performed in all these cases to understand the etiology and nature of hydrops, including the location as well as the amount of fluid collections, amniotic fluid index, placental thickness, fetal echocardiography and Doppler velocimetry (16, 17).

We reported the case of severe immune fetal hydrops in a women at 31 week of pregnancy complicated by maternal D alloimmunization and SLE.

Case Report

A 36-years-old woman pregnant for the third time, was admitted at 31 week of pregnancy at the Obstectrics and Gynaecology Unit of the University Hospital "G. Martino" of Messina to perform a third trimester's ultrasound examination. A severe hydrops in the fetus was identified for the first time. Therefore, she was hospitalized.

In her history three miscarriages and two pregnancies were referred. She also suffered of SLE since 2016. Her blood group was A RhD negative (partner's group was O RhD positive). She reported a physiological course of pregnancy except for a threat of abortion in the first trimester. In this occasion antenatal anti-D prophylaxis were not performed and neither at 28 weeks of

pregnancy, as well as current guidelines in pregnancy suggested [18]. In each month during pregnancy indirect Coombs' test was reported negative. During this period she was treated with acetylsalicylic acid, methylprednisolone and hydroxycloroquine.

At the admission blood evaluation showed positive values of antinuclear antibodies (1:2560) and anti-dsDNA antibodies (1:80). Indirect Coomb's test was also positive (1: 250). The ultrasound examination showed a female fetus, with extremely low fetal movements and regular heartbeats. It was highlighted a polydramnios with a 100 mm of maximum pocket of amniotic fluid, fetal hydrops with ascites and hydrothorax (Fig. 1 and Fig. 2).

Fig. 1. Fetal edema

Fig. 2. Fetal hydrothorax

The fetal growth, due to the edema (Fig. 3), was equivalent to 95° centile. The morphological examination of the fetal anatomy did not detect any malformation. The echocardiographic exam showed a slight pericardial effusion, a regular anatomy of the heart with situs solitus, but in mesocardia due to the hydrotorax. The flow-rate study revealed an incontinence of atrioventricular valves and pulmonary valves.

Fig. 3. Fetal hydrops with ascites and hydrothorax

Doppler velocimetry of the umbilical artery (UA) and middle cerebral artery (MCA) showed a normal value of pulsatility index (UA: PI 1.07; MCA PI 2.27), and a Systolic Peak Velocity (PSV) of the Middle Cerebral Artery (MCA) of 45.51 cm/sec (expected 41.93, mOm 1.09), suggesting for a non-anemic fetus. Given the severity of the clinical picture, the respiratory distress prophylaxis with betametasone was administered, and a caesarean section was planned.

At birth, the newborn presented severe hydrops and she was cyanotic, apneic and the heart rate

was < 100 bpm. According to Newborn Life Support proceedings endotracheal intubation, surfactant intratracheal instillation and chest compression were performed. Furthermore for the presence of persistent cardiorespiratory arrest and drug therapy was administered after umbilical venous catheterization (epinephrine, bolus of 10 ml/kg of normal saline) and, due to a mild anemia (Hemoglobin 10.3 g/dl), O rhD negative red blood cells were transfused. Moreover bilateral thoracocentesis was necessary and, after the insertion of chest tubes in the 4th intercostal space of both chest side, 200 cc of citrine yellow liquid were removed. The Apgar score was 1, 5 and 5, at 1st, 5th and 10th minutes respectively. Nevertheless clinical condition remained extremely critical. At birth, blood gas showed a condition of severe metabolic and respiratory acidosis (pH 6.43, pO2 9.9 mmHg, pCO2 206 mmHg, Base Excess (BE) -35 mmol/l, HCO3- 2.7 mmol/l). When the resuscitation maneuvers were completed, control of breathing was first obtained with mechanical ventilation with SIPPV mode (Synchronized Intermittent Positive Pressure Ventilation) and then with HFOV mode (High Frequency Oscillation Ventilation). Chest X-ray revealed an increased cardio-mediastinal shadow, lifting diaphragm and severe soft tissue edema, ascites and hydrothorax. (Fig. 4).

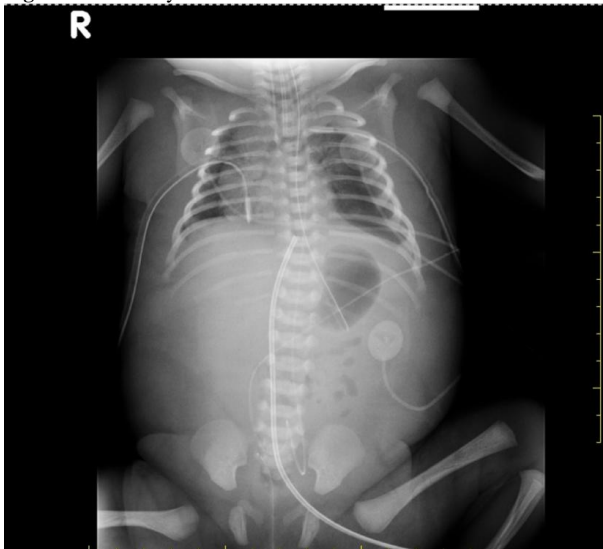**Fig. 4**. Chest X-Ray after few hours from birth.

Fig. 5. Chest X-Rat at the hospital discharge

After 8 hours from birth blood gas showed a persistently severe metabolic and respiratory acidosis (pH 7.02, pO2 43.5 mmHg, pCO2 66.5 mmHg, Base Excess (BE) -15mmol/l, HCO3-12.5mmol/l, Hemoglobin 15.1 g/dl). Due to suspect of pulmonary hypertension caused by the severe pulmonary hypoplasia a treatment with Nitric Oxide and Fenoldopam were administered successfully. Several echocardiograms confirmed the moderate-severe pulmonary hypertension but unexpectedly cardiac pump function was normal. ECG also revealed normal sinus rhythm and a Congenital Heart Block (CHB) was excluded. The progressive improvement of clinical condition allowed to remove the chest tubes and Non-invasive ventilation (NCPAP - HHHNC) was started with a great

response of the infant. (Fig. 5) Neurological evaluation performed by cranial sonography and MRI scan revealed a normal brain. After a month a healthy baby was discharged.

Discussion

Despite improvements in postnatal care such as advanced mechanical ventilation, surfactant treatment, and inhaled nitric oxide, hydrops fetalis (HF) is still a serious fetal condition with high risk of perinatal mortality, morbidity and long-term disability. Some authors report that the number of fluid collection sites are the strongest antenatal ultrasound risk factor for prediction of poor outcome (19, 20). Moreover, the risk of fetal death is higher if fetal hydrops is diagnosed at an earlier gestational age (7).

The severe hydrops we reported could be determined by two maternal risk factors: maternal D alloimmunization and SLE.

In haemolytic disease of the fetus and newborn (HDFN), fetal hydrops occurs when fetal Hb deficit exceeds 7 g/dL. It is interesting to observe that in our case the severe hydrops was not associated with a severe anemia of the newborn. The various mechanisms responsible for hydrops are hypoalbuminemia secondary to depressed liver function, increased capillary permeability, iron overload secondary to hemolysis, and increased venous pressures due to poor cardiac function. Complex genetic factors influence the ability of individuals to respond to red cell antigens. Rh D is the most effective immunogen and, as little as 0.1 to 1 ml of D positive red cells can stimulate antibody production (18). Sensitization is believed to have no adverse health effects for the mother and, the first baby is usually not harmed, as the pregnancy is generally completed by the time that sensitization has occurred. In addition to feto-maternal hemorrhage at birth, events during pregnancy may lead to the production of maternal anti-D antibodies and thus sensitization may also occur during the antenatal period. It has been estimated that approximately half of newborn infants with hemolytic disease are mildly affected, requiring no treatment. Of the remainder, half will become hydropic in utero, and half will be born apparently healthy but without treatment may either die of kernicterus or be left severely disabled (21). In our case, Coombs' test evaluated during pregnancy was mild positive and no fetal anemia was suggested to the PVS in the MCA; these data were confirmed at birth (Hb 10.3 g/dl).

SLE during pregnancy could develop an irreversible 3rd degree heart block in the newborn, consequently hydrops and high risk of death. Anti–52-kd Ro/SSA and anti-La/SSB antibodies have been reported to be more strongly associated with CHB than was anti–60-kd Ro/SSA alone(22). It is considered a pathologic readout of passively acquired autoimmunity consequent to FcRn-mediated placental transport of antibodies reactive with protein components of the SSA⁄Ro-

SSB⁄La ribonucleoprotein complex (23). It carries a significant mortality (20–30%, primarily fetal and neonatal) and morbidity (67% of those surviving affected children require permanent pacing before adulthood) (23). According to the related literature, no difference in mortality, prematurity or degree of final block or need for pacemaker was founded for fetuses treated with or without steroids. It was noted that the presence of either pericardial or pleural effusions as well as ascites and hydrops seemed to improve with the use of steroids(23). Fortunately, in our patience a Congenital Heart Block (CHB) was excluded and ECG revealed a normal sinus rhythm.

Conclusion

We reported an unusual case of severe hydrops due to RhD alloimmunization, although during pregnancy hemoglobin value estimated seemed normal and at birth it revealed only a mild anemia. Nevertheless despite the critical clinical condition at birth, no cardiorespiratory or neurological adverse outcomes occurred.

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