

Hydrops fetalis associated with chorioangioma and thrombosis of umbilical vein

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Placental chorioangioma and thrombosis of an umbilical vein varix are rare etiologic factors of non-immune hydrops fetalis. Herein, we report a patient who had hydrops fetalis associated with placental chorioangioma and thrombosis of an umbilical vein varix. This is the first report of coexistence of non-immune hydrops fetalis with placental chorioangioma and thrombosis of an umbilical vein varix.

Key words: chorioangioma, hydrops fetalis, thrombosis, umbilical vein varix.

Non-immune hydrops (NIH) is an abnormal accumulation of serous fluid in the tissue and body cavities of a fetus secondary to factors other than isoimmunization. This condition is becoming the predominant form of fetal hydrops with the declining frequency of Rh isoimmunization. There are numerous etiologic factors related to NIH. Thrombosis of the umbilical varix and placental chorioangioma are rare causes of these factors¹. We report NIH caused by both thrombosis of an umbilical vein varix and placental chorioangioma. To the best of our knowledge, this is the first such case reported in the literature.

Case Report

A baby girl was born at the 27th week of gestation to a 43-year-old mother by spontaneous vaginal route. Her Apgar scores were 8, 9 and 10 at 1, 5 and 10 minutes, respectively. The parents were not related. She had a healthy brother and sister. At the 25th week of gestation, ultrasound examination showed the presence of polyhydramnios associated with hydrops fetalis findings, which included skin edema and mild pleural and pericardial effusions. In addition, prenatal fetal ultrasonography revealed a dilated intrahepatic umbilical vein and a 70 x 50 mm hypoechoic placental mass. Doppler flow was

present within the mass. Doppler ultrasound showed thrombosis in the umbilical vein and irregular hypervascularization of the placental mass. There was a dilatation of the umbilical vein from the level of the umbilical insertion to the fetal abdomen, up to 10 mm. Doppler flow was normal in the middle cerebral artery. The remainder of the fetal anatomy and cardiac anatomy appeared normal. At the 26th week of gestational age, a cordocentesis was performed to assess the degree of expected anemia, to investigate the hydrops etiology and to exclude fetal chromosomal aberrations. Her mother's blood group type was 0 Rh (+), and the patient's was A Rh (+). The results revealed a normal female karyotype and fetal anemia (hemoglobin level: 9 g/dl), and intrauterine blood transfusion with 0 Rh(-) blood (according to cross-match with mother's blood) was performed. Her birth weight, length and head circumference were 1330 g (75-90p), 34 cm (25-50p), 27 cm (75p), respectively, and were in the normal ranges. After birth on physical examination, the infant did not appear hydropic. The liver was palpable 3 cm below the right costal margin, and the spleen was palpable 1 cm below the left costal margin. There were no signs of respiratory or heart failure, or ascites.

On macroscopic examination, the placenta weighed 1000 g and showed a large, gray spherical mass with a diameter of 7 cm bulging on the fetal surface. The umbilical cord was edematous. Histopathologic examination revealed a vascular tumor surrounded by trophoblastic layer (Fig. 1). In non-tumoral areas, nucleated red blood cells in villous capillaries, focal infarcts and thrombosis in some of the fetal vessels were noted. There was also an acute severe inflammation of extraplacental membranes and chorion. A diagnosis of chorioangioma and chorioamnionitis was made.

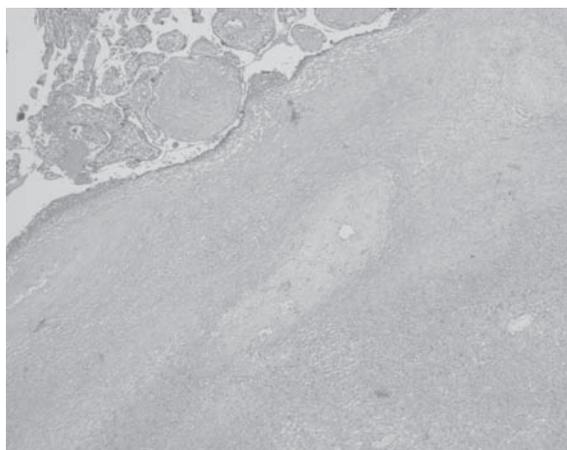


Fig. 1. Chorioangioma: the tumor consists of fibrous stroma and numerous capillaries and is surrounded by trophoblasts (hematoxylin & eosin, x40).

On laboratory studies, hemoglobin was 12.6 g/dl, white blood cell count was 7400/mm³, and platelet count was 104000/mm³ in the cord blood, and reticulocyte count was 20%; normoblast count was 19%. There were hemolytic findings in the blood smear. Direct Coombs test was negative and there was no blood subgroup incompatibility. Cord blood gases and biochemistry analysis were in the normal limits. Serologic studies including toxoplasmosis, cytomegalovirus, rubella and parvovirus infections were found negative.

Color Doppler examination revealed that the umbilical vein was patent and ectatic (Fig. 2). There was a 5.5 X 7.0 mm thrombus in the dilated umbilical vein (Fig. 3). The chest X-ray was normal. The cardiac echocardiography performed on the first postnatal day showed second-degree mitral valve failure, patent ductus arteriosus (2 mm in diameter), normal heart size, and absence of pericardial effusion.



Fig. 2. Color Doppler shows umbilical vein varix and thrombus (arrow).



Fig. 3. Ultrasound image demonstrates the thrombus in the umbilical vein varix.

According to thrombophilia work-up performed in the newborn, immunoglobulin G (IgG) and IgM, anticardiolipin, antiphospholipid, and antibody studies were negative. Factor V Leiden, prothrombin gene and 5, 10-methylenetetrahydrofolate reductase mutation studies were unremarkable. Antithrombin III activity was 71% (normal neonatal range: 40-90%). Protein C activity was 44% (normal neonatal range: 15-65%). Protein S activity was 22% (normal neonatal range: not available). Levels of factor VIII, lipoprotein A and homocysteine were normal. Enzymatic studies of the erythrocytes (glucose-6-phosphatase dehydrogenase, pyruvate kinase) were normal. Thrombophilia work-up of the parents was normal.

During laboratory studies, because of excessive collection of blood from our patient, we performed erythrocyte transfusion due to increasing anemia. Subcutaneous low molecular mass heparin (enoxaparin) (1.5 mg/kg, twice daily) was started for thrombosis². The patient did not have any additional problem in the follow-up. Follow-up on color Doppler

ultrasound performed on the 27th day revealed that the umbilical vein remained patent and ectatic, and there was a 6.0x1.2 mm sized thrombus inside it. Maintenance of low molecular weight heparin treatment was planned. At the postnatal second month, color Doppler ultrasound showed that the thrombus had disappeared.

Discussion

Hydrops fetalis is defined as the accumulation of excessive extracellular fluid manifesting with edema, ascites, and pleural and pericardial effusions in a fetus. It is usually classified into immune and NIH based on the presence or absence of fetal anemia secondary to red cell alloimmunization, respectively¹. There are more than 100 conditions associated with NIH. Among these associations are chromosomal abnormalities, cardiovascular abnormalities, lymphatic obstructions, hematological abnormalities, infections, vascular lesions including umbilical vein thrombosis, and tumors, especially large chorioangioma. Disorders of the cardiovascular system are the most frequent underlying causes of NIH, followed by chromosomal abnormalities. Tumors and vascular abnormalities are extremely rare causes of NIH^{1,3-5}.

Placental chorioangioma is a primary benign tumor with predominantly vascular involvement. This tumor is probably a hamartoma derived from the primitive chorionic mesenchyme or has a neoplastic origin. These placental tumors are mostly small, often microscopic, and are found in 1% of all placentas undergoing careful and systematic histopathological examination. Large chorioangioma >5 cm in diameter is rare but significant in a clinical respect. It occurs in about one per 3,500-9,000 births, and may lead to the development of severe anemia, thrombocytopenia, cardiac decompensation, and NIH. Anemia may be a result of fetomaternal hemorrhage, microangiopathic hemolysis, or hemodilution. Thrombocytopenia may develop by the trapping of blood cells in the angiomatous tumor and hemodilution. Heart failure develops due to the cardiac output increase to ensure a sufficient output through the low resistance shunt caused by the chorioangioma, and venous return to the right side of the heart is also increased. All of these factors may lead to NIH. NIH is related to the size of the

tumor⁶⁻⁸. Anemia and thrombocytopenia in our case could be explained as the effects of the chorioangioma.

Varix of the intra-abdominal portion of the fetal umbilical vein is a very rare anomaly. It has been associated with intrauterine death and hydrops fetalis, but differences in fetal outcome vary widely. These different outcomes may be explained by several factors. In general, the outcome for fetuses affected by varix of the umbilical vein is unknown, and the relationship between umbilical vein varix and NIH is unclear⁶⁻¹⁰. Probably, the umbilical vein varix may have functioned as an arteriovenous shunt, leading to cardiac overload and cardiac failure that can cause hydrops fetalis in fetal life¹¹. As the thrombophilia work-up on the infant was normal, thrombosis of the umbilical vein varix may have developed due to turbulence in the flow of blood. In the post-gestational period, absence of the baby's severe anemia and effusion is likely to be related to the IU erythrocyte transfusion.

In conclusion, this is the first report of coexistence of non-immune hydrops fetalis with placental chorioangioma and thrombosis of an umbilical vein varix. The association between these clinical entities should be remembered, as it may have clinical importance in the management of the patients.

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