Human Parvovirus B19 Associated Non-Immune Hydrops Fetalis

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Non-immune hydrops fetalis (NIHF) in a relatively rare syndrome associated with different etiologies, usually due to chromosomal aberrations or cardiac anomalies. Human parvovirus B 19 (HPV B 19) associated intrauterine infections. NIHF and fetal loss have been reported lately[1]. HPV B19 passes through the placenta and infects eiythroid progenitor cells with subsequent lysis, anemia and hydrops. Fetal liver cells may be infected at the same time. The rate of HPV B 19 infection in NIHF cases is unknown but estimated to be about 10%[2]. In anautopsy series, HPV B19 was found in 0.7% of all cases and in 16% of hydropic cases[3]. We present a non-irnmune hydrops case, which was due to HPV B 19 infection and discuss the recent issues governing this disease.

Case Report

O.B. was born as a second child of his family, after a gestation of 35 weeks. The mother had her first antenatal ultrasound examination at the 28th week and the baby was hydropic at that time. Cordocentesis revealed hemoglobin concentration of 8.8 g/dl, leucocyte count of 10.000/mm^3, platelet count of 124 .000/mm^3 and a negative indirect coombs test. The liverenzymes (AST, ALT) were within normal limits. Close observation and monitoring was planned. The karyotype analysis revealed 46 XY Toxoplasma, rubella, cytomegalovirus and herpes virus antibodies were negative. Therefore, the baby was evaluated as non-immune hydrops fetalis.

On admission to the neonatal intensive care unit, the physical examination of the baby revealed a weight of 3500 g (>90th centile), length of 47cm (50thcentile). head circumference of 36 cm (50th centile) and abdominal circumference of 36cm (>9Othcentile). He had mild tachypnea and dyspnea and normal breath sounds. The abdomen was flat with a frog-like appearance and liver was 2 cm palpable below the right costal margin. The examination of cardiovascular and other systems were unremarkable.

Laboratory investigations were: Hematocnt: 60%, Hemoglobin 18.5 g/dl. White blood cells: 10.600/mm^3, platelets: 175.000/mm^3, reticulocytes: 1.2%, indirect coombs test negative, serum albumin 4.4 g/dl, AST: 78 UIL and ALT: 20 U/L. Anteroposterior chest x- ray and the echocardiogram were nonnal. Abdominal ultrasound revealed moderate ascites and grade II renal stasis, which was thought to be due to the ascites. Repeat toxoplasma, rubella, cytomegalovirus and herpes virus antibodies were negative but antiparvovirus B19 IgM and IgO were positive. Non-immune hydrops of the baby was thought to be secondary to HPV B 19 infection, No intervention but close monitoring of the baby was planned.

On his first foflow-upvisitat 1 month, he was doing well and there was a slight increase (0.5 cm) in the abdominal circumference. By ultrasonographic examination, there was mild ascites.

At second month, the abdominal circumference had increased to 38.6 cm with a hepatornegaly of 7 cm. and splenomegaly of 8 cm below the respective costal margins. Renal function was normal, total serum protein was 5.8 g/dl, albumin 3.2 g/dl, AST: 73 U/L. ALT: 46 U/L, Anti-parvovirus B 19 IgM was positive but IgG was negative. The amount of ascites had increased.

At third month, there was not an increase in the size of the liver and spleen ascites was minimal but the

abdominal circumference was 40.6 cm. He was growing in his appropriate centile. On the fourth month, the hepatomegalv had regressed to 1.5 cm and splenomegalv to 4 cm. with minimal ascitcs. His hematocrit was 32%. Serum levels of total IgA. IgO, 1gM and IgE were within normal limits. Antiparvovirus B 19 IgM was still positive but IgG was negative. The infant is still being followed up.

Discussion

Non-immune hydrops has different causes including hematologic, cardiovascular, pulmonary. renal, infectious causes and congenital anomalies involving the mother, fetus or placenta: or it may be totally idiopathic.

Relation of panvovirus infection and fetal losses had long been recognized in animals but the first human case of hydrops was reported in 1984 by Brown et al during a fifth disease epidemic[4]. The risk ofa young woman getting infected with HBVB 19 is 50% if there is another one within the family as a carrier and 15% if there is carrier within the working environment[2]. The true risk of maternal HPV B 19 infection to the fetus is unknown[5]. In a prospective study involving 1967 pregnant women, antibody titre were screened routinely and 3.3% of them were found to have IgM. There were no pathological findings in 95% of them whereas one had an abortion and 4% babies were small for gestational age[6]. Intrauterine infection with HBV B19 has one of three consequences: 1) Fetal death, non-immune hydrops or abortion; 2) Self limited infection. The infection is eradicated by the antibody developed by the fetus or mother.; 3) Persistent or recurrent subclinical infection. The reasons and the rate of this kind of infections are unknown[7]. In a prospective study, lasting 3.5 years, designed to disclose the outcome of fetal infection, it was found that 84% cases had uneventful births, whereas 14% had fetal loss[8]. Fetal loss was generally encountered in the second trimester. The risk of fetal loss is 15% in the first trimester and 17% in the second trimester[9]. In another prospective studies, average fetal loss was about 10%[10]. In antibody studies carried out in healthy newborns and in hybridization studies in fetal tissues, fetal HBV B19 infection was found in one-third of cases of maternal infection8. Similar results have been reported fronivirological studies[9]. HPV B19 infection does not lead to specific congenital malformations. Only one fetus had an occular malformation and which may have been due to the intense inflammatory reaction[11].

The main site of involvement in the fetus is bone marrow Reduction in the erythrocyte production may result in anemia and congestive heart failure. Erythroblastic infiltration may also lead to portal hypertension and hepalic insufficiency which contributes to the development of iivdrops. Direct cardiac injwy by the virus itself may also contribute to this process. Hydrops is usually clinically evident between 18th to 27th week, on average 21st week[12].

Fetal infection may be monitored by ultrasonography or maternal serum aipha-feto protein levels. Serum alpha fetoprotein levels rise 4 weeks earlier than the first ultrasonographic changes in the fetus[9]. Packed red cell transfusion are effective in the treatment of hydrops. The risks of intrauterine transfusion should be considered because in some cases, hydrops may regress spontaneously without any complications. These are sometimes referred as transient, subclinical or spontaneously regressive types[13-15]. Therefore, risk and benefit ratio of intrauterine transfusions should be a major concern and the decision to transfuse should be taken cautiously[16].

The diagnosis of infection depends on showing specific IgM and IgG in patient sera by the enzyme-linked immunosorbent assay (ELISA) technique. This method is still reliable[17] and the specificity and sensitivity of positive IgM by ELISA is higher than 98%[18]. Detection of viral DNA by the polymemse chain reaction (PCR) technique is also diagnostic. This technique was not available in our unit; but since the ELISA method was highly sensitive, we decided to use it as a diagnostic tool.

Intrauterine infection related cytopema was obvious in our patient. However, post-natal cytopenia was not observed. The baby received limited amount of fluids and did not require transfUsions. Specific 1gM was still positive in the fourth month which implied that infectious process was still going on. However, IgG was negative during the same period, which could be due to the relative immune deficiency in the baby. Perinatal recovery of IgG from the baby was most probably due to passive transfer through the placenta. IgG plays the major part in neutralization of the virus and in long term immunity, which develops within a few days in patients with a good immunity. Chronic infection is associated with chronic reticulocytopenia and anemia[20]. In 3 to 4 month old babies, IgG production may not be high enough to prevent infection and persistence of infection may be expected in these babies, which has been the case in this baby. Increment of ascites and hepatomegaly together with hypoproteinemia, seen in this patient were also observed in other chronically ill patients and with the increase in liver enzymes. All these manifestations reflect the involvement of the liver. Slight anemia may be due to the same reason. In some cases, hypogammaglobulinemia has been reported with congenital anemia and these respond well to immunoglobulin therapy[21].

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