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Letters to the editor

Mirror syndrome due to coxackie B virus associated to maternal peripartum cardiomyopathy

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Sir,

The so-called "Mirror syndrome" (MS) still remains a rare and debatable condition, usually diagnozed when maternal impairment occurs as a direct consequence of fetal pathology.

We report a case of MS in a 34-year-old Caucasian woman, gravida 0, para 0, blood type A, rhesus-negative, referred to our University Hospital at 26+5 weeks' gestation because of fetal hydrops. The fetus underwent a detailed II level ultrasound and showed severe fetal hydrops including ascites, pericardial effusion, polyhydramnios, skin and placental edema (thickness >6 cm). Fetal echocardiogram was normal. Doppler evaluation of the middle cerebral artery (MCA) peak systolic velocity (PSV) [8] was performed and the value was 70.5 cm/s, with an estimated fetal hemoglobin of 4.09 g/dL. The evaluation of suspected severe fetal anemia included indirect Coombs' test and a sero-analyses. All tests were negative, except positive serology for coxackie B virus (CBV) IgM antibodies. Infection was confirmed by the detection of viral RNA. Both C-reactive protein and total white blood cell count (WBC) were normal. The woman presented normal blood pressure and diuresis. A dilution anemia was present, with a low hemoglobin of 8.7 g/dL, hematocrit 25%, plasma protein 44.6 g/L and serum albumin 20 g/L, the latter was corrected with 40 g of albumin.

The next day, an intrauterine fetal blood transfusion was performed and after 24 h MCA-PVS was 23 cm/s and estimated fetal hemoglobin was 13 g/dL.

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Mirror syndrome was suspected because of both maternal and fetal hydrops and maternal hemodilution. Over the next three days, maternal conditions revealed a progressive generalized marked edema, diuresis of 500 mL/24 h, albumin 19 g/L, hemoglobin 7.6 g/dL, antithrombin III 66%. Two-thousand UI of antithrombin III and 40 g of albumin were administered. At 27 weeks and 3 days the woman developed signs and symptoms of heart failure: deep hypotension, cyanosis and generalized edema of the neck, abdomen and vulva. An emergent cesarean section was performed.

The female neonate weight was 1290 g, appeared edematous, hypotonic and pale with Apgar score of 5 at the 5th minute, Hb 7.8 g/dL, pH 7.05, Htc 18%. Neonatal serum resulted positive for IgM CBV antibody, but negative for viral RNA. Due to rapid worsening of clinical setting, orotracheal intubation and mechanical ventilation were performed and the newborn was transferred to the Neonatal Intensive Cure Unit. An evacuative paracentesis was performed, obtaining 50 mL of ascites. The newborn's condition improved progressively and after two months was transferred to the Pediatric Unit. Placental weight was 490 g and histological examination revealed stromal villous alterations because of marginal subtrophoblastic edema. Umbilical cord also appeared edematous. No inflammation was present in the amniochorion.

After cesarean section, the woman was transferred to the Cardiac Care Unit. Cardiac ultrasonography examination showed that the left ventricular wall motion was reduced and left ventricular ejection fraction decreased. Left ventricular dimensions were mildly increased and pleural effusions were present. Peripartum cardiomyopathy (PPCM) diagnosis was based upon the clinical presentation of congestive heart failure and objective evidence of left ventricular systolic dysfunction. Under close care, her cardiac function recovered gradually. The woman was discharged on the 17th postpartum day from the hospital with the diagnosis of myocarditis. The histological diagnosis on cardiac biopsy was compatible with an active linfocitarian peripartum myocarditis. Hypertension and consistent proteinuria were absent in this case, although described in about half of the cases of mirror syndrome [10].

In addition to generalized edema, the patient presented other associated findings: increased uric acid level, hypoproteinemia and dilutional anemia (low hemoglobin and hematocrit without hemolysis). Based on hemodilu-

tion, MS has been differentiated from the usual pre-eclamptic syndromes [4].

Renal dysfunction is another finding associated to MS, but in this case restricted diuresis was present later, because of cardiac failure development.

In the present case, Doppler evaluation of the MCA-PSV diagnosed fetal anemia causing fetal hydrops and an *in utero* fetal blood transfusion was immediately performed.

Hydrops fetalis detected by ultrasonography was found in two cases of CBV fetal infection [3, 6]. Interestingly, in this case, the fetal heart had no specific lesion of myocarditis, as newborns infected with CBV may have severe clinical or pathological myocardial involvement [2].

The treatment of choice for MS is based on the cause of fetal hydrops and upon the maternal conditions [5]. In the present case, impaired maternal conditions did not allow expectant management, although fetal anemia was corrected. At birth, fetal anemia was confirmed and blood transfusions were required to correct the persistent anemia.

Peripartum cardiomyopathy (PPCM) is relatively rare, but a life-threatening disease that in the majority of cases occurs after delivery. Moreover, the etiology still remains controversial, despite that the proposed causes include myocarditis, abnormal immune response to pregnancy, and maladaptation to the hemodynamic stresses of pregnancy, as well as stress activated cytokines, viral infection, and prolonged tocolysis [1]. The physiologic and hemodynamic changes of pregnancy may result in an increased susceptibility to viral myocarditis, higher body load of virus (such as coxsackie and echovirus), and worsening of myocardial viral lesions [7].

Nakamura et al. previously described another case of PPCM occurring in the postpartum period of mirror syndrome associated with severe fetal cardiac anomalies, hypothesizing that alteration of maternal hemodynamics by fetal cardiac anomalies might have some effect on the development of PPCM in the postpartum period [9].

In conclusion, although maternal prognosis of MS is usually good after termination of pregnancy, in the present case the occurrence of PPCM made the maternal prognosis uncertain. In fact, particular attention should be addressed to exclude that causative factors of the MS may play a role in the development of other maternal pathologies, such as in the case of infections.

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