CAS CLINIQUE / CASE REPORT

WHEN THE MIRROR'S IMAGE DECEIVES
A Case Review

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ABSTRACT • Introduction : Since the 19th century when Ballantyne first described the association of fetal hydrops, placental edema and maternal systemic manifestations, mirror syndrome has implied a lot of controversy about delivery recommendations due to associated fetal and maternal risks. **Case**: In our article we describe a case of nonimmune hydrops fetalis whereupon delivery of the fetus the maternal clinical status was stable and completely recovered from her condition. **Discussion**: Mirror syndrome and preeclampsia seem to be reflected by a similar fan of signs and symptoms, with a thin line of differences and consequences, leading to confusion affecting treatment and management decisions. **Conclusion**: Unaddressed, mirror syndrome can lead to significant maternal and fetal complications, yet conservative management can be attempted to reverse the condition, unlike preeclampsia; therefore, thorough evaluation and individualization of each case should be done.

Keywords : mirror syndrome; hydrops fetalis; placental edema; preeclampsia

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RÉSUMÉ • Introduction : Au XIXe siècle Ballantyne fut le premier à décrire l'association entre l'anasarque fœtal, l'œdème placentaire et les symptômes maternels systémiques. Depuis, le syndrome miroir suscite un bon nombre de controverses concernant les recommandations de délivrance. Cela est dû à la gravité du pronostic fœtal et à l'augmentation de la morbidité et de la mortalité maternelle. **Étude de cas :** Dans notre article, nous décrivons un cas d'anasarque fœtal non immun où l'état clinique de la mère est devenu tout à fait stable après la délivrance du fœtus. **Discussion** : La prééclampsie et le syndrome miroir présentent plusieurs signes et symptômes similaires. Cela contribue à une confusion de diagnostics affectant foncièrement le traitement ainsi que la prise de décisions. **Conclusion** : Le syndrome miroir conduit à des complications au niveau de l'état clinique de la mère et du fœtus. D'où la nécessité d'une évaluation pertinente et d'une étude particulière et indépendante de chaque cas.

Mots-clés : anasarque fœtal; œdème placentaire; syndrome miroir; prééclampsie

INTRODUCTION

Pseudotoxemia, maternal hydrops syndrome, pregnancy toxemia, acute second trimester gestosis, early onset preeclampsia, maternal hydrops syndrome, triple edema or mirror syndrome are all different titles of one single uncommon and frequently underdiagnosed disease entity [1,2].

John W. Ballantyne in 1892 was the pioneer describing the association of maternal edema in pregnancy with fetal and placental hydrops secondary to Rhesus isoimmunization [3,4] while Potter described the same association between the mother and her fetus in the absence of iso-immunization, an entity called nonimmune hydrops fetalis (NIHF). The term mirror syndrome per se was introduced in 1956 by O'Driscoll [5,6].

Mirror syndrome is defined as a dramatic complication of fetal hydrops (generalized edema, pleural or pericardial effusions, and placental thickening) leading to clinical maternal preeclampsia or preeclampsia-like symptoms (edema, elevated blood pressure, proteinuria, abnormal liver function tests and abnormal platelet count), afterwards [7].

Uncommonly, mirror syndrome resolves with treatment and improvement of the hydrops of the affected fetus, despite the fact that some causes are inherently uncorrectable [8,11]. The definitive treatment of mirror syndrome so far is similar to severe preeclampsia and comprises the delivery in accordance with gestational age [7].

CASE

A 24-year-old patient, G4P3A0, of blood group A, Rhesus positive, was referred at 28+1 weeks of gestation with elevated blood pressure readings. In a peripheral clinic, and during her 8th visit, the patient was found to have blood pressure readings of 180/100 mmHg. Smooth pregnancy course was noted prior to this incident with no reported findings of previous ultrasounds and no morphology scan was done before.

Upon presentation, the patient had already received a total of 10 g $MgSO_4$ (6 g IM and 4 g IV) with a 1000 mg of methyldopa (Aldomet 500 mg 2 tablets) and a Foley catheter inserted. On physical examination she was drowsy but

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cooperative and oriented to time, space and person with a blood pressure of 140/90.

Cardiopulmonary exam was within normal limits despite a poor inspiratory effort.

The abdomen was soft with a gravid uterus and a fundal height of 32 cm. Bilateral lower limb pitting edema was noted up to the knees. Deep tendon reflexes were present bilaterally.

The patient's past medical and past surgical histories were unremarkable. Her obstetrical history was notable for two prior intrauterine fetal demises of male fetuses at 7th month of gestation (of unknown causes) delivered vaginally, adding one-term vaginal delivery of a male baby with neonatal death at the 2nd day of life also due to unknown reasons.

Ultrasound done upon presentation showed hydrops fetalis with ascites, subcutaneous edema, and polyhydramnios with an estimated weight of 1300 g. Placentomegaly was also noted.

Initial labs done upon admission reflected normal complete blood count with no hemoconcentration (Hb 11.3 - Ht 34.3 - Plt 215) with normal liver and kidney function (BUN 7.5 - creatinine 0.55 - uric acid 5.81 - SGOT 18 - LDH 273) and a magnesium level of 3.62. Urine analysis was only significant for +1 protein, with negative nitrite and leukocyte esterase.

Pelvic exam showed a closed posterior thick cervix.

Fetal monitoring showed minimal beat to beat variability with recurrent variable subtle decelerations.

Tocography showed irregular contractions of low amplitude.

Decision to induce labor was taken based on the suspicion of severe preeclampsia with misoprostol (Cytotec) 50 micrograms vaginally switched to oxytocin (Pitocin) after 4 hours. Penicillin G was started for GBS prophylaxis (5 million IU loading and 2.5 million IU every 4 hours as maintenance until delivery), betamethasone for fetal lung maturity (Diprofos 14 mg, two injections IM 12 hrs apart) and magnesium sulfate was continued for seizure prophylaxis and fetal neuroprotection at a rate of 2 g per hour IV drip, under close observation in the delivery suite.

Twelve hours after the beginning of induction, the patient delivered by spontaneous vaginal delivery a live male baby of Apgar score 5 then 0 at 1 and 5 minutes respectively. The baby was intubated and transferred to the NICU in respiratory distress; he did not pass urine or meconium, and passed away after around 6 hours with blood cultures being negative. The placenta was removed manually and was found to be massive; cultures were taken and placenta was sent to pathology. Misoprostol 400 micrograms was continued q4hrs for suspected retained tissue. Magnesium sulfate for seizure prophylaxis was continued for 24 hours postpartum at a rate of 2 g per hour IV drip. She was transferred to the regular floor afterwards in a stable clinical and hemodynamic condition.

The patient throughout her stay had a blood pressure of 120/85 ± 100 mmHg with good urine output. A slight decrease in the lower limb edema was noted. Labs repeated on day one postpartum were stable showing normal blood pressure and liver function (Hb 11.9 - Hct 36.2 - Plt 286 - uric acid 6.8 - SGOT 20.02 - LDH 334.86).

The placental culture was insignificantly positive for coagulase negative staphylococci (CoNS). HBsAg, HCV-Ab and HIV 1 & 2 Ab were all negative.

Blood tests for toxoplasma, parvovirus, herpes as well as the karyotype were not done for financial reasons.

Placental pathology showed hydropic changes of villi with delayed maturation, intravillous trophoblastic inclusions suggestive of aneuploidy but no viral inclusions were seen.

The patient was discharged home on day 3 postpartum in a stable condition both clinically and hemodynamically.

She was counselled on the importance of follow-up.

DISCUSSION

Deceiving is the single best word to describe the mirror syndrome. Distinguishing between mirror syndrome and preeclampsia is obviously difficult. The low incidence of this syndrome, the absence of large series of published cases and the wide variety of maternal presentations make the definitive diagnosis as well as the mode of treatment, expectant versus terminal, a challenge.

The number of reported cases of mirror syndrome is limited, with the incidence of the syndrome being both under diagnosed and under reported.

Thorsten Braum *et al*. did the first complete review of mirror syndrome, which included 56 reported cases between 1956 and 2009. It showed that the mirror syndrome is related to fetal hydrops and large placental mass reflected by maternal symptoms with weight gain and maternal edema (89.3%) followed by elevated blood pressure (60.7%), mild anemia and hemodilution (46.4%), albuminuria and proteinuria (42.9%), elevated uric acid and creatinine (25%), mild elevated liver enzymes (19.6%), oliguria (16.1%), headache and visual disturbances (14.3%) and low platelets count (7.1%) [4].

Faced by the overlap of similar signs and symptoms between preeclampsia and mirror syndrome, several authors tried to propose methods to differentiate between the two. The presence of maternal hemodilution and mild anemia seems to be the most distinguishing feature capable of differentiating mirror syndrome from preeclampsia as hemoconcentration is a typical pathophysiological feature in preeclampsia. Still, in several clinical situations, it is unreliable [1-12].

In our case, the initial presentation with the hypertension and marked lower limb edema draws attention towards preeclampsia with severe features. This justifies the initiation of magnesium sulfate for both seizure as well as neuroprophylaxis. The findings of the ultrasound consistent with hydrops fetalis and placentomegaly make the image less clear since no obvious culprit was highlighted

especially that the patient was supposedly well followed. The workup antepartum came back negative with modest +1 protein on urine analysis which was more or less inconclusive for the diagnosis. However, the final pathology report of the placenta raised suspicion for aneuploidy, a known cause for hydrops fetalis, and thus pointing fingers towards mirror syndrome as a final diagnosis. Not to forget that the patient had no previous history of preeclampsia. It is true that the whole workup for an undisputable diagnosis was hindered by financial/religious reasons as well as missing information regarding her previous intrauterine fetal demise (IUFD) and neonatal death, but we can safely conclude that this particular case is more or less clear. A karyotype in this case, performed on the umbilical cord insertion or fetal Achilles tendon, might have helped in the final diagnosis as well as clarifying her past obstetrical history. It was noted in our case that the patient's clinical and hemodynamic status improved after delivery, which also goes along with the features of mirror syndrome.

The pathophysiology of the syndrome is thought to be the consequence of the fetal hydrops. It is well known that hydrops fetalis can be induced by a wide variety of insults including Rhesus iso-immunization, multiple pregnancies, viral infections, fetal malformations, fetal and placental tumors and fetal arrhythmias.

Both, the immune and nonimmune causes, are associated with villous edema. This leads to high intracellular placental water content, compression of the villous blood vessels and impaired oxygen exchange compromising the fetal oxygen and blood supply [13-15]. This process leads to increased production and release of sVEGFR-1 (and other anti-angiogenic factors) into the maternal circulation. Excessive concentrations of these products would then be responsible for maternal edema and endothelial cell dysfunction in those cases complicated with preeclampsia [16]. The above mentioned changes were reinforced with placental histological examinations which revealed immature intermediate villi with edematous changes, increased syncytial knots with increased staining with antibodies against sVEGFR-1, increased intervillous fibrin, and multifocal villous calcifications, all not found in normal or preterm cases [16].

Similar to the diagnosis, the treatment of these cases with mirror syndrome remains controversial and challenging as well. Several cases reported showed that once the cause of hydrops is treated and the fetal hydrops improved, maternal symptoms might disappear. One of these cases was fetal bladder outlet obstruction complicated by maternal mirror syndrome. It was followed by resolution of the symptoms after relieving the massive urinary ascites via peritoneo-amniotic shunt [17]. In another case, selective termination of a hydropic fetus in a twin-twin transfusion syndrome relieved maternal hypertension and severe peripheral edema [18,19]. Maternal treatment with diuretics, calcium channel blockers and β-blockers, in a case of parvovirus B19 induced mirror syndrome complicated by severe maternal pulmonary edema, had resolved maternal symptoms [20].

Adequate treatment of fetal tachycardia in cases of cardiac failure induced hydrops resulted in an improvement of fetal cardiac function and reduction in fetal hydrops resulted in an improvement of fetal cardiac function and reduction in fetal hydrops as well as maternal edema [21,22]. Prenatal diagnosis of Diamond-Blackfan anemia and intrauterine transfusion led to the resolution of the mirror syndrome [23]. In our case, there was no clear cause for the patient's presentation to be addressed and treated conservatively, so the decision to proceed with delivery was the best option to undertake in order to save the mother's life at least.

CONCLUSION

Finally and despite the above mentioned cases, the delivery of the fetus remains the only way to reverse maternal symptoms and to overcome or avoid severe complications as happened in our case, or if attempts at treating to resolve the hydrops fail. Lack of diagnosis, unclear histories, or deceiving presentations leave us obstetricians facing a dilemma: to treat or not to treat? Such an unclear horizon for a deceiving not so common disease: the mirror syndrome.

Photos were not attached due to the refusal of the patient [and absence of her consent].

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