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Case Report

Mirror Syndrome: A Case Report and Overview of Literature

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ABSTRACT

Mirror syndrome or Ballantyne syndrome describes an association of maternal edema and hydrops fetalis. Due to it's presentation, it is often misdiagnosed as preeclampsia even though there are several differences in clinical presentation, pathophysiology, prognosis and treatment. We present a case of early mirror syndrome at a gestational age of 19 weeks and 2 days. Our patient who was in a consanguineous relationship with her husband presented with severe edema, a weight gain of 7 kg in one week and severe headaches. She had a slightly elevated bloodpressure and a mild proteinuria. Ultrasound revealed significant hydrops fetalis and a large placenta. The diagnosis of early mirror syndrome was suspected and she was transferred to a tertiary referral centre. There maternal and fetal workup could not reveal the etiology of the hydrops fetalis. A decision for termination of pregnancy was made because of the poor fetal and maternal prognosis due to the early presentation and the unknown etiology. After the delivery all the symptoms resolved spontaneously.

With this case report, our first aim is to clarify the clinical presentation of mirror syndrome in early second trimester. Second we aim to provide information to help diagnose this syndrome and to make the distinction with preeclampsia, the other early hypertensive disorder in pregnancy.

Keywords: Idiopathic hydrops fetalis, Mirror syndrome, Ballantyne syndrome, Maternal edema, Preeclampsia

Introduction

Mirror syndrome, also known as Ballantyne syndrome, triple edema or early onset preeclampsia [1,2] is a syndrome characterized by the development of maternal edema in association with hydrops fetalis. It was first described in 1892 by John W Ballantyne as a syndrome causing hydrops fetalis due to severe rhesus immunization [3]. The incidence of Ballantyne syndrome is not clear. Although it's a rare condition, it is now clear that several other causes of immune and non-immune hydrops fetalis like viral infection (parvovirus, cytomegalovirus), twin-to-twin transfusion syndrome, fetal arrythmia, fetal malformations (aneurysm of the vein of Galen, Ebstein's anomaly) and fetal or placental tumors (sacrococcygeal tumor, placental chorioangioma) are linked to the development of mirror syndrome [2,4-10]. It is believed that mirror syndrome can be caused by any etiology that induces fetal hydrops with significant fetoplacental disfunction [11]. In approximately 30% of the cases, the etiology of fetal hydrops remains unknown [12].

Mirror syndrome is a rare entity and because of it's clinical presentation it is often misdiagnosed as preeclampsia. We report a case of mirror syndrome early in second trimester with unknown etiology. Our first aim is to clarify the clinical presentation of mirror syndrome in early second trimester. Second, we aim to provide information to help diagnose this syndrome and to make the distinction with preeclampsia.

Case Report

A 30 year old primigravida, was referred to our emergency department with complaints of rapidly progressive edema and severe headaches at a gestational age of 19 weeks and 2 days. The symptoms started 2 weeks earlier.

The patient was in a consanguineous relationship with her husband. Initial maternal evaluation revealed edema of both the upper and lower extremities and the face. She had gained 7 kg in 1 week. Her blood pressure was elevated (145/95mmHg). A urine sample showed mild proteinuria. Other vital signs were normal, with an oxygen saturation of 99%. Lung auscultation was normal, no chest X ray or cardiac ultrasound examination was made.

Laboratory results showed: bloodtype B rhesus D positive, rhesus c positive, irregular antibodies negative, haemoglobin 7.2 mg/dl, haematocrit 0,35L/L, platelet count 285 x 10^9 g/l, uric acid 0.30 mmol/l, alanine aminotransferase 27 U/l, HCG >600000. Fetal ultrasound showed hydrops fetalis with severe ascites, mild pericardial effusion, mild edema of the subcutaneus tissue and placentamegaly (>4cm). She was diagnosed with mirror syndrome and we transferred her to a tertiary referral center for further diagnosis.

In the tertiary referral center advanced ultrasound examination showed no other major structural abnormalities nor fetal arrhythmia. Doppler examination showed a normal pulsatility index in the umbilical artery and the middle cerebral artery (no signs of fetal anemia). Amniocentesis was performed and showed no known unbalanced chromosomal abberations or aneuploidy but there were several runs of homozygosity (ROH) >5Mb (marker for consanguinity) that can cause autosomal recessive diseases. Maternal serology was negative for toxoplasmosis, rubellavirus, cytomegalovirus, herpes simplex-virus and syphilis.

Due to the known poor prognosis of hydrops fetalis at this gestational age, a termination of pregnancy to prevent deteriorating maternal morbidity or even mortality was discussed interdisciplinary and with the couple. The pregnancy was initially managed expectantly at the request of the parents. Three days after the diagnosis of the hydrops fetalis and mirror syndrome a termination of pregnancy was performed by vaginal administration of prostaglandins. She delivered a stillborn boy of 305 gr. Besides the prenatal diagnosed hydrops fetalis, obduction of the fetus and pathologic examination of the placenta could not confirm a specific cause of the hydrops foetalis. Within a few days after delivery the maternal symptoms resolved after which she was discharged from the hospital.

Discussion

Mirror syndrome is a rare syndrome where the mother mimics the fetoplacental edema [3], therefore the key feature is maternal edema (80-100%). Other symptoms are hypertension (57-78%), headache, visual disturbances (14%) and proteinuria (20-56%) . Laboratory clues of mirror syndrome are mild anemia, low haematocrite, mild proteinuria, elevated uric acid and creatinine, slightly abnormal liver function, oliguria and very high serum human chorion gonadotrophin (HCG) [7].

The distinction between mirror syndrome and preeclampsia can be difficult due to similar symptoms. However, there are some differences in clinical presentation and examinations (Table 1). Regarding the clinical presentation, in mirror syndrome hypertension is usually not very high and proteinuria is usually mild in contrast to preeclampsia. Regarding the findings on examination in mirror syndrome there is usually a polyhydramnion and a large placenta on ultrasound examination in contrast to oligohydramnion with a small for gestational age fetus in preeclampsia [13-15]. In the laboratory findings the main difference is a low haematocrite without haemolysis in mirror syndrome and a high haematocrite with haemolysis in preeclampsia. The thrombocyte count is usually normal in mirror syndrome [1,2,16].

Table 1: Differences in clinical presentation and examination between mirror syndrome and preeclampsia.

	Mirror syndrome	Preeclampsia
Clinical	- Severe edema - Mild hypertension	- Mild to severe edema - Mild to severe hypertension
Laboratory	- Low haematocrite - Mild proteinuria - Elevated uric acid - Elevated creatinine - Abnormal liverenzymes - Oliguria - Normal thrombocyte count - Very high HCG	- High haematocrite - Mild to severe proteinuria - Elevated uric acid - Elevated creatinine - Abnormal liverenzymes - Oliguria - Thrombocytopenia is possible
Ultrasound	- Polyhydramnion - Hydrops fetalis - Placentamegaly	- Oligohydramnion - Fetal growth restriction possible

The postulated pathogenesis is another difference between mirror syndrome and preeclampsia. Although the pathogenesis is not entirely clear, there are several theories. The fact that maternal morbidity resolves when the placental edema diminishes, advocates a placental origine of the syndrome [5,17]. Some Studies suggest the theory of hyperplacentosis in mirror syndrome with an enlarged placenta, hydropic chorionic villi, overactivity and immaturity of the trophoblast (reflected in high HCG levels) and persistence of the Langhans's layer. In contrast, in pre-eclampsia there's hypoplacentosis with a small placenta that shows zones of infarction and decreased functional activity. Secondary to that, intra-uterine growth restriction of the fetus [13]. As opposed to preeclampsia, where endothelial damage is likely the origin of pathology, in mirror syndrome the endothelium is intact at first. Only later, when endothelial damage appears, mirror syndrome can progress to preeclampsia.

In general the fetal prognosis in mirror syndrome is poor because the syndrome usually develops when there is already severe fetoplacental edema and dysfunction [13]. Intra-uterine death or stillbirth occurs in 56% of the cases probably caused by high-output cardiac failure of the fetus due to fluid overload [2,16]. Some causes of hydrops fetalis are treatable and could lead to a decrease of the placental hydrops and to reversibility of the fetal and maternal morbidity and mortality [5].

There is also a significant maternal morbidity and mortality risk. Possible complications are the development of severe (pre)eclampsia, pulmonary edema or maternal heart failure [18]. Some experts report an elevated risk of post partum hemorrhage and amniotic fluid embolism [19]. The maternal symptoms disappear 5 to 14 days after delivery [20]. In this case of very early mirror syndrome of unknown etiology the only therapeutic option is to terminate the pregnancy. In more advanced pregancies case reports described several treatments with good fetal and maternal prognosis. A French case report described 2 cases of mirror syndrome in hydrops fetalis caused by an infection with parvovirus where the maternal morbidity diminished and a healthy baby was born after fetal blood transfusion by means of

cordocentesis [21]. Others report an improvement of symptoms after chemical treatment of fetal arrythmia with flécaïnide®. Resolution of the syndrome in twin to twin transfusion syndrome (TTTS) is also described, when selective feticide of the hydropic fetus in a dichorionic diamniotic twin pregnancy is performed. Others report drainage of the peritoneal-, thoracal of abdominal hydrops, and even spontaneous resolution after a parvovirus infection [5].

Conclusion

Mirror syndrome is a rare condition, especially in early second trimester, and is characterized by maternal edema in association with fetal hydrops of any etiology. We present a case of mirror syndrome in early second trimester. After 3 days, the pregnancy was terminated due to the poor fetal prognosis and deteriorating maternal condition. Obstetricians and midwifes should be aware that this condition can occur early in pregnancy and treatment should be offered immediately. Although the decision to terminate a pregnancy at a non viable gestational age is very difficult, it is often the only therapeutic option to prevent further maternal morbidity and even mortality in case of early second trimester mirror syndrome.

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