

## Mirror Image Syndrome: 1 Case and Literature Review

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### Abstract

Mirror image syndrome is a triad of maternal, fetal and placental edema, which is a rare disease. In this paper, a clinical case of a patient with mirror syndrome admitted to our hospital in 2023 was reviewed, and relevant literature at home and abroad was analyzed, in order to improve the clinical understanding of mirror syndrome, so as to early diagnosis and treatment, and improve the prognosis of mother and child.

**Keywords:** mirror image syndrome, fetal edema syndrome, prenatal diagnosis, preeclampsia

### 1. Case Report

A 25-year-old female patient, G1P0, was admitted to the hospital on January 20, 2023, due to the discovery of systemic fetal edema for 1 day at 33+2 weeks gestation. Regular prenatal checkups during pregnancy. No history of toxic exposure during early pregnancy. Cervical zona pellucida (NT) examination results at 12+2 weeks of pregnancy: 1.4mm, non-invasive prenatal screening hints: low risk. Oral glucose tolerance test was performed at 24+5 weeks of gestation, and the results were 5.8-9.0-8.7mmol/L. The pregnant women did not monitor their blood glucose regularly by themselves, and the four-dimensional single fetus was suggested in our hospital at 26+1 weeks of gestation. Hyperamniotic fluid (AFI 279mm); Placenta racquet. 26+5 weeks of pregnancy due to ultrasound: infundibular changes of cervical tube hospitalized for fetal preservation treatment, after admission to monitor the large profile of blood sugar, indicating that blood sugar control. Prenatal examination at 27+2 weeks of gestation showed ultrasonography: amniotic fluid index of 273mm; prenatal examination at 28 weeks of gestation showed ultrasonography: amniotic fluid index of 326mm; amniotic fluid reduction by amniocentesis was performed, fetal chromosome karyotype and low coverage large-scale parallel sequencing technology (CNV-seq) were detected, and no intrauterine infection pathogens were detected in amniotic fluid. Pregnant women have normal blood pressure before pregnancy and stable blood pressure during pregnancy. Pregnant women denied hypertension, coronary heart disease and other acute and chronic history. Menarche 15 years old, regular menstruation, cycle 30 days, volume, no dysmenorrhea, the last menstruation on June 1, 2022. Physical examination after admission: the general condition was OK, the vital signs were stable, the blood pressure was 120/70mmHg, and there was no edema in both lower limbs. Specialist examination: uterine height 42cm, abdominal circumference 115cm, fetal position ROT, fetal heart rate 146 times/min, uterine orifice not open, no palpation. Admission ultrasound: single fetus; Double paracardial diameter 89mm, head circumference 309mm, abdominal circumference 374mm, femur length 62mm, amniotic fluid index 393mm, maximum amniotic fluid depth 125mm, stomach bubble shape is not full, size about 31mm×11mm, liver echo rough and reduced. Fetal body skin and subcutaneous soft tissue edema, head, face, trunk for. A large amount of free fluid can be seen in the chest cavity, about 53mm deep on the left side and 51mm deep on the right side. The venous catheter flow frequency was a three-phase wave, located in the same direction as the baseline, and the A-wave deepened, S/a 3.48. Admission diagnosis: 1) Pregnancy with fetal edema; 2) Fetal ultrasound soft index is positive; 3) Pregnancy combined with excessive amniotic fluid; 4) 33+2 weeks of pregnancy (G1P0ROT); 5) Gestational diabetes.

After admission, fetal heart rate, intake and loss, weight changes, vital signs were monitored, dexamethasone was given to promote fetal lung maturation, magnesium sulfate fetal brain protection and other treatments. After hospitalization, relevant examinations were improved: blood routine WBC  $12.06 \times 10^9/L$ , Hb  $119g/L$ . Coagulation function: D-Dimer  $1.69mg/LFEU$ . Urine protein negative. Liver function: Total protein  $59g/L$ , albumin  $34.5g/L$ , alanine aminotransferase  $8.9U/L$ , aspartate aminotransferase  $15.8U/L$ . Renal function: creatinine  $40.8\mu mol/L$ . 24-hour albuminuria quantification:  $0.16g$ . TROCH tested positive for herpes simplex virus I IgG antibody, negative for IgM antibody, positive for rubella virus IgG antibody, negative for IgM antibody, positive for Cytomegalovirus IgG antibody, negative for IgM antibody. Maternal blood type O, RH-negative. Conjugal blood group antibody titer 1:4. On the second day of admission (33+4 weeks of gestation), fetal abdominal and cardiothoracic MRI was performed, indicating: single fetus, head position, abdominal fluid accumulation, excessive amniotic fluid, enlarged heart shadow, bilateral pleural effusion with non-distension of both lungs. On the 3rd day of admission, the patient presented with sunken edema of subcutaneous tissue of the ankle, edema +. On the 6th day of admission, the blood pressure rose to  $139/93mmHg$  in the morning and  $115/76mmHg$  was remeasured 2 hours later. On the 7th day of admission (34+2 weeks of gestation), the pregnant woman occasionally had vaginal discharge, a small amount of white vaginal discharge could be seen through the speculum implanted during physical examination, the PH test paper was blue, and the fetal membrane was broken early. On the same day, the blood pressure was elevated, up to  $142/92mmHg$ , accompanied by edema and sunken edema of both lower limbs, edema ++, considering the mirror syndrome, the risk of continuing pregnancy was greater, so the lower section of the abdominal uterus was performed under combined epidural anesthesia. Intraoperative: clear color of amniotic fluid, about  $3500ml$ . A live baby girl weighing  $4340g$  was delivered with ROA. General edema, abdominal distention, Apgar score 3, no spontaneous respiration, endotracheal intubation transferred to neonatology.

After the operation, anti-infection, contraction-promoting, blood pressure lowering treatment was given, the edema of both lower limbs was significantly reduced, and the fifth day after the operation, the recovery was good. Postoperative pathological findings: 1) Local villi adhesion of placenta, dilation and congestion of small villi vessels, multi-focal fibrinoid deposition, small focal infarction and calcification. A small amount of lymphocyte infiltration in the fetal membrane. The umbilical vessels are congested and bleeding. 2) Leiomyoma (uterine myomatoid nodules) with red deformation. (placenta) Mild to moderate intervillous edema on the maternal surface, mild focal intervillous edema on the fetal surface, and submembranous local interstitial edema.

## 2. Literature Review

Mirror image syndrome is a kind of rare disease, which is a comprehensive clinical manifestation of different degree of maternal edema and blood dilution secondary to fetal edema and placental edema.

### 2.1 Etiology

Any factor that causes placental and fetal edema may lead to mirror syndrome. Mirror syndrome may be caused by hypoxia of the trophoblast due to placental villous edema, which increases the production of specific biomarkers, resulting in an imbalance of angiogenic factors and anti-angiogenic factors, further leading to maternal endothelial damage. Some studies have suggested that the increase of HCG concentration can lead to placental ischemic necrosis, and HCG can directly release aldosterone by stimulating the luteinizing hormone receptor expressed in the adrenal gland, resulting in the increase of maternal plasma aldosterone concentration leading to maternal edema and blood dilution (Umazume Takeshi, MORIKAWA Mamoru, YAMADA Takahiro, et al., 2016).

Both immune and non-immune fetal edema can lead to maternal mirror syndrome. Common diseases because: RH maternal blood type incompatibility; Abnormal fetal cardiovascular development; Twin transfusion syndrome; Intrauterine parvovirus B19 infection; Fetal malformations, fetal and placental tumors; Metabolic disease; Hematological diseases, etc. Chromosomal abnormalities and genetic factors related to monogenic diseases can lead to non-immune fetal edema, with 45, X being the most common, followed by trisomy 21 and trisomy 18 (WALLER K, CHAITHONGWONGWATTHANA S, YAMASMIT W, et al., 2005). It has been reported that in cases of fetal edema syndrome, fetal edema occurring at gestational week greater than 24 weeks and placental thickening are suspected risk factors for mirror syndrome (HAN Zhenyan, CHEN Xiaodan, WANG Qingqing, et al., 2021).

### 2.2 Clinical Features

Mirror image syndrome develops rapidly, the clinical understanding of the disease is insufficient, the diagnosis is delayed, the treatment is poor, and the prognosis is often poor. Mirror image syndrome usually presents as fetal edema, placental edema and secondary maternal edema in clinic. The mother will show varying degrees of edema, followed by elevated blood pressure, mild anemia, blood dilution, mildly elevated liver enzymes, proteinuria, etc. The most serious is maternal pulmonary edema (ALLARAKIA S, KHAYAT H A, KARAMI M

M, et al., 2017). Most of the symptoms of edema and hypertension in pregnant women disappear spontaneously after fetal edema is improved or pregnancy is terminated.

Mirror syndrome associated with proteinuria and high blood pressure can appear similar to preeclampsia. Preeclampsia is a pregnancy-induced hypertension syndrome involving multiple systems in the mother. Currently, the pathogenesis is not clear. The well-recognized theory is that the dysplasia and dysfunction of placenta and the release of various active factors by the placenta into the maternal blood circulation lead to the injury of maternal vascular endothelium and the imbalance of vasoconstriction and dilation. Hypertension and impaired maternal multiple organ function eventually occur (Chappell Lucy C, Cluver Catherine A, Kingdom John, et al., 2021). There are similar clinical manifestations between preeclampsia and mirror syndrome, which can be distinguished from the following: (1) Mirror syndrome progresses from fetal edema and is related to the onset of fetal edema syndrome, and preeclampsia is defined as appearing after 20 weeks of gestation. (2) Mirror syndrome may be manifested as hemodilution, anemia, and hypoproteinemia due to increased circulating blood volume (HAN Zhenyan, CHEN Xiaodan, WANG Qingqing, et al., 2021). Preeclampsia is usually characterized by blood concentration and decreased effective blood volume. It is therefore recommended to obtain baseline hemoglobin levels at the onset of fetal edema to help determine the development of hemodilution. Weekly CBC, CMP, UPC, LDH, and albumin tests may also be performed to assess the natural history of mirror syndrome. Maternal weight was assessed 1-2 times a week to monitor maternal weight gain (Biswas Sonia, Gomez Julie, Horgan Rebecca, et al., 2023). (3) Mirror syndrome Maternal symptoms of mirror syndrome can be significantly improved after fetal edema and placental edema are corrected. Preeclampsia needs active symptomatic treatment and timely termination of pregnancy can be improved.

### *2.3 Treatment of Mirror Syndrome*

Mirror syndrome is a rare obstetric complication with a high perinatal mortality. Clinicians should actively search for etiology and symptomatic treatment, correct fetal edema in time, and terminate pregnancy in time (Caroline Ruth Mathias & Carmela Rizvi, 2019). Remission of maternal symptoms and improvement of perinatal prognosis are based on remission of fetal edema, regardless of etiology (LLURBA E, MARSAL G, SANCHEZ O, et al., 2012). Fetal edema associated with parvovirus B19 infection is secondary to fetal anemia, especially in the first trimester when parvovirus infection leads to a greater risk of fetal edema, which may be caused by the virus crossing the placenta leading to fetal anemia. Desvinges et al. (2011) described a case of mirror syndrome secondary to fetal edema caused by parvovirus B19 infection. After the treatment of intrauterine fetal blood transfusion, the symptoms of fetal systemic edema subsided and the maternal condition was also improved. A pregnant woman diagnosed with twin transfusion syndrome at 21+5 weeks of gestation was treated with fetal laser technology. Three days after surgery, she was readmitted to hospital due to edema of both lower limbs of the pregnant woman, and then underwent intrauterine transfusion. After treatment, fetal edema subsided and symptoms of maternal mirror syndrome improved (Ahmed A. Nassr., 2017). In a case of giant chorionic angioma with fetal edema, severe fetal anemia, mild cardiac hypertrophy, hyperdynamic cardiac circulation, and maternal mirror syndrome were presented. Intrauterine blood transfusion and amniotic fluid drainage were performed at 29 weeks of gestation, and the conditions of the fetus and the mother further deteriorated, leading to delivery at 29+5 weeks of gestation, and the newborn died 3 hours after birth (García-Díaz Lutgado, Carreto Práxedes, Costa-Pereira Susana, et al., 2012).

In this case, the patient's disease developed rapidly, with ultrasound indicating excessive amniotic fluid at 26+5 weeks of gestation, which gradually progressed to fetal edema, and mirror syndrome at 34+2 weeks of gestation. At the 28th week of pregnancy, the amniotic fluid index was 326mm, and amniotic fluid reduction was performed by amniocentesis, and 1280ml amniotic fluid was extracted from the amniotic cavity. The ultrasound examination on the 7th day after surgery indicated that the amniotic fluid index was 217mm. Amniocentesis can release part of the amniotic fluid, which can effectively relieve the discomfort of pregnant women caused by excessive amniotic fluid and improve the living environment of the fetus. However, there is no strong evidence whether the operation can effectively delay the occurrence of fetal edema. In summary, this case should be a warning to clinicians: (1) for unexplained excess amniotic fluid during pregnancy and fetal abdominal circumference greater than the actual gestational week, great attention should be paid to shorten the interval of ultrasound examination. If the possibility of fetal edema is considered, intrauterine treatment should be actively performed. (2) In case of excessive weight gain in pregnant women in the late stage, various reasons should be considered. (3) After full evaluation, if the patient loses the opportunity for intrauterine treatment, timely termination of pregnancy can improve the prognosis of mother and child.

Procedural interventions to correct fetal edema include maternal blood transfusion, intrauterine blood transfusion, amniocentesis, laser ablation, peritoneal amniotic shunt, thoracic amniotic shunt, and aortic valve dilation. Correction of fetal edema has significant correlation with fetal survival. However, if intrauterine treatment cannot be performed and the mother's condition worsens, the pregnancy needs to be terminated in time (TELES

A T A, CZERESNIA R, ELREFAEI A, et al., 2021), especially in the face of critical maternal conditions, labor must be organized urgently. In a retrospective study, 29% of patients with fetal edema developed mirror syndrome, which is more common in early severe fetal edema and can cause blood dilution and elevated serum hCG (HIRATA Go, Aoki Shigeru, SAKAMAKI Kentaro, et al., 2016). In a national study, 85 out of 98,484 pregnant women who delivered had fetal edema. Among the cases of fetal edema, 16 cases developed mirror syndrome, and the incidence of mirror syndrome was 0.0162% (CHEN Ruiyun, LIU min, YAN Jianying, et al., 2020). The incidence of mirror image syndrome is slightly higher in cases of fetal edema, and there is a lack of effective prevention and intervention measures, which needs attention. Through ultrasound screening of the thickness of the transparent layer of the fetal neck and the screening of fetal structural abnormalities in the early pregnancy, attention to the possibility of fetal edema syndrome in the early pregnancy can effectively avoid the later maternal edema and reduce the occurrence of mirror syndrome.

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