Clin. Lab. 2024;70:XXX-XXX

CASE REPORT

Mirror Syndrome Combined with Postpartum Hemolytic Uremic Syndrome

Ning Luo, Hong J. Li, Zhu Lin, Yin Li, Hong M. Gao

Department of Critical Care Medicine, Tianjin First Central Hospital, Tianjin, China

SUMMARY

Background: **Mirror syndrome is a rare disease characterized by "triple edema", while Hemolytic Uremic Syndrome (PHUS) is a serious disease that occurs within a short period of time after the end of pregnancy, with a low prevalence and poor prognosis, and it is even rarer for both to occur in the same patient.**
Methods: **We report a case of mirror syndrome combined with PHUS and analyze the clinical data to improve the understanding of the disease.**
Results: **The patient presented clinically with "triple edema" and was diagnosed with mirror image syndrome. After cesarean section, the patient developed cardiac insufficiency, renal insufficiency, hemolysis, and other symptoms and was diagnosed as PHUS. After active treatment, the maternal prognosis was good.**
Conclusions: **Mirror syndrome and PHUS are both clinically rare diseases with poor long-term prognosis if not diagnosed and treated in a timely manner; therefore, awareness of the diseases, early and accurate diagnosis and timely and correct treatment should be improved.**
(Clin. Lab. 2024;70:xx-xx. DOI: 10.7754/Clin.Lab.2024.240229)

Correspondence:
Ning Luo
Tianjin First Central Hospital
Tianjin
China
Phone: +86 13752764132
Email: loloningning@163.com

KEYWORDS

mirror syndrome, Postpartum Hemolytic Uremic Syndrome, edema, acute heart failure, plasma exchange

CASE REPORT

The patient, 33 years old, presented to the Obstetrics Department of Tianjin First Central Hospital on September 17th, 2022, at 23:00 with the chief complaint of "G1P0, gestational age 28 + 6 weeks, lower limb edema for three days, and proteinuria detected for 7 hours." The patient had a history of good health. Mid-pregnancy ultrasound revealed uneven echogenic masses in the fetal liver (vascular tumor? Approximately 55 x 26 x 41 mm). Further examination was recommended, and termination of pregnancy was advised if necessary. Blood pressure remained stable during pregnancy. Three days before admission, the patient developed left lower limb edema, and two days before admission, right lower limb edema appeared. On the day of admission, the patient visited the outpatient department of our hospital. Ultrasound indicated "fetal cardiomegaly, subcutaneous ede-

Case Report accepted February 25, 2024

ma in the fetus, and thickening of the placenta." Urinalysis showed "2+ protein," and blood routine revealed WBC 8.94 x 10^9/L, HGB 92 g/L, and PTL 84 x 10^9/L. The patient was admitted to our Obstetrics Department for further diagnosis and treatment. On admission, the vital signs were as follows: temperature 36.7°C, pulse 80 beats/minute, respiratory rate 16 breaths/minute, and blood pressure 136/80 mmHg. Specialized Examination in Obstetrics: Gynecological examination revealed a uterine height of 35 cm, abdominal circumference of 101 cm, LOA fetal position, vertex presentation, floating engagement, no uterine contractions, intact membranes, fetal heart rate of 140 beats/minute, and external pelvic measurements [24]-[28]-[20]-[8.5] cm. Laboratory and auxiliary examinations before admission: Early pregnancy liver function was normal, and the five hepatitis B indicators were normal. Syphilis, hepatitis C antibodies, and HIV were all negative. On September 17th, 2022, our hospital's obstetric ultrasound revealed a biparietal diameter of 79 mm, head circumference of 275 mm, abdominal circumference of 339 mm, femur length of 53 mm, Grade I placenta with a thickness of approximately 69 mm, S/D ratio of 2.4, amniotic fluid depth of 52 mm, and a floating umbilical cord visible in the fetal neck (U-shaped impression). The fetal thoracic cavity appeared slightly narrow, and the fetal thoracic-to-cardiac ratio was approximately 0.68. The abdominal cavity was enlarged, and a strong echogenic mass measuring about 97 x 73 x 80 mm was observed inside, with unclear boundaries, uneven internal echogenicity, a close relationship with the liver, and visible blood flow signals circulating it. A few blood flow signals were observed inside (Figure 1). Conclusion: Singleton in cephalic presentation with a large echogenic mass in the fetal abdominal cavity, fetal cardiomegaly, subcutaneous edema in the fetus, and thickening of the placenta. Admission Diagnosis: 1. Primigravida, 28 + 6 weeks gestation, 2. Mirror syndrome, 3. Fetal intra-abdominal mass: hepatic hemangioma? 4. Moderate anemia complicates pregnancy. Subsequent comprehensive laboratory tests upon admission revealed creatinine 126 μmol/L, albumin 22.3 g/L, D-dimer 8,575.13 μg/L, and 24-hour urine protein quantification of 1.94 g. Echocardiography showed mild mitral and tricuspid regurgitation. Fetal magnetic resonance imaging (MRI) indicated a massive occupying lesion in the fetal liver, suggesting a high likelihood of fetal hepatic hemangioendothelioma. The fetus exhibited an enlarged cardiac silhouette, subcutaneous edema, and thickening and edema of the placenta. On the day of admission, the patient received a transfusion of 20 g human albumin, resulting in diuresis and partial relief of lower limb edema. On September 18th, hemoglobin (HGB) was rechecked and found to be 81 g/L, and platelet count (PLT) was 69 x 10^9/L. Preoperative preparations were completed, and two therapeutic doses of apheresis platelets were transfused. At 3:25 AM on September 19th, a cesarean section was performed. Postoperatively, in the recovery room, HGB was 80 g/L, PLT was 78 x 10^9/L, and two units of packed red blood cells were transfused. At 8:30 AM on September 19th, the patient was transferred back to the obstetric ward with a blood pressure of 145/97 mmHg. At 2:30 PM on the same day, the patient experienced mild shortness of breath, receiving a 20 mg intravenous injection of furosemide; however, there was no significant increase in urine output. At 4:30 PM, the patient developed chest tightness and respiratory distress, with a blood pressure of 162/107 mmHg and peripheral oxygen saturation of 80%. Symptoms progressively worsened, leading to rapid transfer to the Intensive Care Unit (ICU). Upon admission to the ICU, the parturient exhibited a heart rate of 145 beats/minute, respiratory rate of 18 breaths/minute, blood pressure of 167/100 mmHg, unmeasurable peripheral oxygen saturation, blurred consciousness, evident dyspnea, cyanosis in the face and peripheral limbs, bilateral moist rales throughout the lungs, audible heart sounds with regular rhythm and 2+ edema in both lower limbs. Immediate measures included endotracheal intubation and assisted ventilation with a respirator. Blood gas analysis revealed a pH of 7.17, $PaCO_2$ of 40 mmHg, PaO_2 of 100 mmHg, HCO_3- of 14.6 mmol/L, BE of -13.2 mmol/L, and lactate (Lac) of 3.9 mmol/L (fiO_2 100%, PEEP 8 cmH_2O). Considering the possibility of acute heart failure, the patient received inotropic support, diuretics, and coronary artery dilation therapy. While symptoms improved and oxygenation slightly improved, the patient remained oliguric. Bedside ultrasound revealed widespread B-lines in both lungs, and Picco monitoring indicated a cardiac index (CI) of 2.2 L/minute/m^2, global end-diastolic index (GEDI) of 721 mL/m^2, and extravascular lung water index (ELWI) of 15 mL/kg. Blood purification therapy was initiated at the bedside. Over three consecutive days of bedside continuous renal replacement therapy (CRRT), with a total ultrafiltration volume of 9,000 mL, the parturient did not experience further episodes of heart failure. However, renal function did not improve, and the 24-hour urine output decreased from 600 mL to 7 mL. On September 23rd, creatinine was 176 μmol/L, hemoglobin was 78 g/L, and platelets were 23 x 10^9/L. Lactate dehydrogenase was 1,842.7 U/L, and reticulocyte percentage was 6.05%. Fragmented red blood cells were observed in the blood smear (Figure 2). ADAMTS 13 activity testing showed 34%, and the Kums test was negative. At this point, hemolytic-uremic syndrome (HUS) was considered, and intravenous steroids and bedside plasma exchange were immediately initiated. The patient's spontaneous breathing stabilized, fluid overload decreased, and on September 27th, the endotracheal tube was removed. From September 29th, the 24-hour urine output exceeded 1,000 mL, gradually entering the diuretic phase. On October 4th, creatinine gradually decreased, and bedside hemofiltration was discontinued. The patient's hemoglobin progressively declined, intermittent transfusions of washed red blood cells were administered, and from October 4th, a gradual stabilization and rise were observed. Steroids were administered intravenously for a total of 20 days and

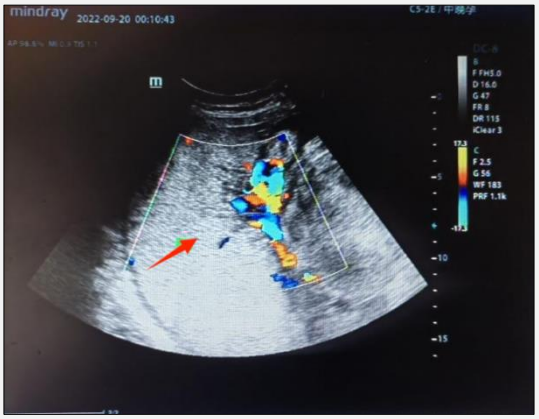

Figure 1. Obstetric ultrasound results: Significant placental edema.

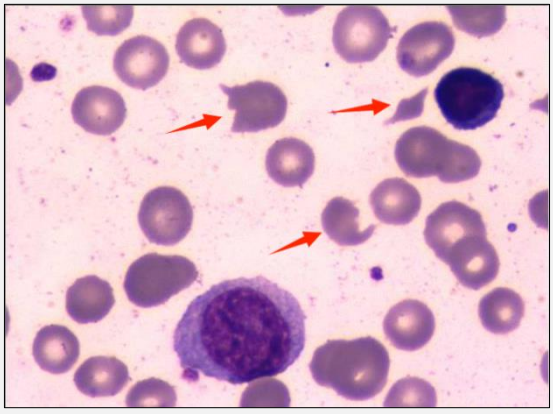

Figure 2. Blood smear results: Fragmented red blood cells were observed in the blood smear.

orally for 23 days before discontinuation. Plasma exchange was performed ten times, with each exchange volume being 2,000 mL. The patient's condition gradually improved, and by October 12th, creatinine was 80 µmol/L, hemoglobin was 89 g/L, and platelets were 218 x 10^9/L. The patient improved and was discharged. Follow-up after two months showed the patient in general good health, with outpatient creatinine at 61 µmol/L, hemoglobin at 106 g/L, platelets at 252 x 10^9/L, and a 24-hour urine protein quantification of 0.79 g.

DISCUSSION

Mirror syndrome is a rare medical condition with a high fetal mortality rate of up to 67.2%. Its primary clinical features include "triple edema," characterized by generalized maternal edema, placental edema, and fetal edema. The etiology is not fully understood but is typically associated with fetal edema, which can be caused by various factors such as infection, immune response, fetal anomalies, fetal or placental abnormalities, and twin-to-twin transfusion syndrome, among others. Maternal signs typically involve edema, hypertension, and proteinuria. Severe complications, including pulmonary

edema, occur in 21.4% of mothers [1]. A retrospective study revealed significant elevations in uric acid, lactate dehydrogenase, creatinine, and D-dimer levels ($p < 0.05$) in pregnant women with mirror syndrome. In contrast, hemoglobin, serum albumin levels, hematocrit values, and platelet counts significantly decreased ($p < 0.05$) [2].

Due to the rarity of mirror syndrome, treatment approaches may vary depending on the specific circumstances. Treatment typically hinges on addressing the underlying cause of fetal edema. If the cause is removable, intervention may alleviate symptoms in both the mother and the infant. In the presented case, the patient was diagnosed with evident "triple edema." However, as the fetal cause was challenging to eliminate, symptoms in both the fetus and the mother progressively worsened, leading to acute heart failure in the mother shortly after childbirth.

Hemolytic Uremic Syndrome (HUS) is a disease characterized by microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure as its primary clinical features. Based on different etiologies, it can be classified into typical HUS and atypical HUS (aHUS). Postpartum Hemolytic Uremic Syndrome (PHUS) is a subtype of aHUS, accounting for approximately 10 - 20% of all cases of aHUS [3]. PHUS typically presents with acute renal failure and intravascular hemolysis shortly after the end of pregnancy. If not promptly diagnosed and treated, some patients may progress to chronic kidney disease.

The pathogenesis of PHUS is not fully understood, but current research indicates that dysregulation of the complement alternative pathway is a significant risk factor for aHUS [4,5]. Patients with complement gene mutations have a higher frequency of requiring dialysis, and their long-term prognosis is worse. The incidence and recurrence rates of progressing to end-stage renal disease are significantly higher in patients with complement gene mutations than those without mutations [3]. Regarding the treatment of PHUS, although studies suggest that plasma therapy does not improve long-term renal outcomes in PHUS patients, both plasma-exchanged and non-plasma-exchanged patients have a similarly high risk (approximately 50%) of developing end-stage renal disease. Plasma therapy remains a widely used empirical treatment, especially when access to eculizumab, a monoclonal anti-C5 antibody, is challenging. Eculizumab has been proven effective in achieving disease remission [6].

CONCLUSION

Mirror syndrome and PHUS are both clinically rare diseases, and their occurrence in the same patient is even more uncommon. The patient showed favorable clinical outcomes with plasma exchange therapy in this case. However, continued follow-up is necessary to obtain relevant information on the long-term prognosis, contributing to the treatment guidance for similar patients. In the future, more information conducive to clinical diagnosis and treatment can be obtained through further pathological and pathophysiological research. We hope that through this case, everyone can increase their awareness of the two diseases, avoid misdiagnosis, and improve patient prognosis.

Acknowledgment:
We would like to thank the other members of the Department of Critical Care Medicine of the First Central Hospital of Tianjin for their constructive criticism.

Source of Support:
This work was supported by the Tianjin Medical Construction of Key Discipline (Specialty) Funded Project (TJYXZDXK-013A).

Ethical Approval:
The study was approved by the Ethics Committee of Tianjin First Central Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained.

Declaration of Interest:
No conflicts of interest.

References:

1. Braun T, Brauer M, Fuchs I, et al. Mirror syndrome: a systematic review of fetal associated conditions, maternal presentation and perinatal outcome. Fetal Diagn Ther 2010;27(4):191-203. (PMID: 20357423)

2. Chen R, Liu M, Yan J, et al. Clinical characteristics of mirror syndrome: a retrospective study of 16 cases. J Obstet Gynaecol 2021;41(1):73-6. (PMID: 32420780)

3. Bruel A, Kavanagh D, Noris M, et al. Hemolytic Uremic Syndrome in Pregnancy and Postpartum. Clin J Am Soc Nephrol 2017;12(8):1237-47. (PMID: 28596415)

4. Fremeaux-Bacchi V, Fakhouri F, Garnier A, et al. Genetics and outcome of atypical hemolytic uremic syndrome: a nationwide French series comparing children and adults. Clin J Am Soc Nephrol 2013;8(4):554-62. (PMID: 23307876)

5. Noris M, Caprioli J, Bresin E, et al. Relative role of genetic complement abnormalities in sporadic and familial aHUS and their impact on clinical phenotype. Clin J Am Soc Nephrol 2010;5(10): 1844-59. (PMID: 20595690)

6. Gupta M, Govindappagari S, Burwick RM. Pregnancy-Associated Atypical Hemolytic Uremic Syndrome: A Systematic Review. Obstet Gynecol 2020;135(1):46-58. (PMID: 31809447)