Published in final edited form as:

A A Pract. 2019 June 15; 12(11): 447–451. doi:10.1213/XAA.0000000000000965.

Maternal Mirror Syndrome Masquerading as Congestive Heart Failure: A Case Report

Wen Xu, MD*, C. Tyler Smith, MD*, Anna Binstock, MD†, Grace Lim, MD, MSc‡,§

*Department of Anesthesiology and Perioperative Medicine, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania

†Department of Obstetrics & Gynecology, Division of Maternal Fetal Medicine, University of Pittsburgh Medical Center, Magee-Womens Hospital of UPMC, Pittsburgh, Pennsylvania

‡Department of Anesthesiology and Perioperative Medicine, University of Pittsburgh Medical Center, Magee-Womens Hospital of UPMC, Pittsburgh, Pennsylvania

§Magee-Womens Research Institute, Pittsburgh, Pennsylvania.

Abstract

Mirror syndrome is a rare pregnancy complication, life-threatening to mother and fetus. Increasing survival rates of congenital heart disease into reproductive age mean that complications like Mirror syndrome in this population may be more challenging to diagnose, given overlapping signs of edema in cases of heart failure exacerbation. We report a case of a pregnant woman with a history of unspecified congenital heart disease, presenting with swelling and distension, with diagnostic findings not consistent with preeclampsia. Her course was complicated by dyspnea, oliguria, and fetal hydrops. A cesarean delivery under neuraxial anesthesia was performed. We review the clinical manifestations of Mirror syndrome and discuss anesthetic and obstetric management considerations for this condition.

Mirror syndrome, also known as Ballantyne syndrome or triple edema, is a rare clinical syndrome in which maternal and placental edema develop in association with fetal hydrops, resulting in significant maternal and fetal morbidity and mortality. The condition has been reported in association with many different causes of fetal hydrops, isoimmunization, and

Address correspondence to Grace Lim, MD, MSc, Department of Anesthesiology, Magee-Womens Hospital of UPMC, University of Pittsburgh School of Medicine, 300 Halket St, Suite 3510, Pittsburgh, PA 15213. limkg2@upmc.edu.

The authors declare no conflicts of interest.

Supplemental digital content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website (www.cases-anesthesia-analgesia.org).

DISCLOSURES

Name: Wen Xu, MD.

Contribution: This author helped write the manuscript.

Name: C. Tyler Smith, MD.

Contribution: This author helped write the manuscript.

Name: Anna Binstock, MD.

Contribution: This author helped write the manuscript.

Name: Grace Lim, MD, MSc.

Contribution: This author helped write the manuscript.

This manuscript was handled by: Kent H. Rehfeldt, MD.

twin–twin transfusion syndrome, although no clear etiology has been elucidated. We present a case of Mirror syndrome in the setting of known maternal congenital heart disease with risk for congestive heart failure. Special considerations for obstetric, anesthetic, and perioperative management are presented. A written Health Insurance Portability and Accountability Act authorization and consent for publication were obtained for this report.

CASE DESCRIPTION

A 24-year-old G1P0 woman, singleton gestation, with limited prenatal care and an initial history of unspecified congenital heart disease status after repair in childhood, presented to a community hospital at 34 weeks and 5 days gestation for increasing lower extremity edema (bilateral feet and lower legs) and abdominal distension. Fetal ultrasound showed polyhydramnios, thickened placenta, and estimated fetal weight of 3900 g (97th percentile; Figure 1). The fetus had significant generalized skin edema, bilateral pleural effusion, possible pericardial effusion, small amount of ascites, hepatosplenomegaly, suspected hepatic calcifications, and suspected intracranial calcifications (Figure 2). Notably, fetal ultrasound was normal at a previous routine 29-week prenatal visit. A biophysical profile is a prenatal ultrasound evaluation that looks at 5 components of fetal well-being: fetal heart rate (HR), fetal breathing, fetal movement, fetal tone, and amniotic fluid volume, with a score of 2 (normal) or 0 (abnormal). The biophysical profile was 4/10. The patient was transferred to our tertiary care high-risk maternity center for further management.

On admission, routine laboratory examination was within normal limits (Supplemental Digital Content, Table S1, <http://links.lww.com/AACR/A246>). Maternal blood type was rhesus positive with a negative antibody screen. Fetal middle cerebral artery Doppler measurements for fetal anemia were unable to be obtained due to significant fetal skin edema. In the absence of any source of isoimmunization causing fetal anemia, cordocentesis and intrauterine transfusion were not pursued, with plans for expectant management. The following day, the patient was found to have a worsening edema extending from the feet to the lower thorax, new dyspnea, and oliguria. Stat formal transthoracic echocardiogram was notable for an abnormal septal motion consistent with postsurgical changes, bicuspid aortic valve, and normal biventricular function; structure and function were grossly normal, and the etiology of the murmur was attributed to the bicuspid aortic valve. Inferior vena cava was collapsible. Chest x-ray was significant for pulmonary congestion. Fetal echocardiogram was normal. Fetal HR showed a category II tracing. Maternal blood type was A Rh positive and antibody screen negative. Given maternal, fetal, and placental edema in the absence of a more likely explanation, the diagnosis of Mirror syndrome was made. After a discussion involving cardiology, obstetrics, and anesthesiology, a joint decision was made to proceed with cesarean delivery due to large estimated fetal weight, maternal volume overload, oliguria, and development of Mirror syndrome. The neonatology team was alerted and present for the delivery.

On preanesthesia evaluation, the patient was afebrile, with a HR of 88 beats/min, blood pressure 119/72 mm Hg, respiratory rate 16 breaths/min, and oxygen saturation of 100% on room air. Height was 145 cm and weight 51.5 kg. She had a III/VI systolic murmur at the left upper sternal border, jugular venous pulsation of 14 cm, and prominently distended

external jugular and scalp veins. Lower body edema extended from bilateral feet up to the lower thorax. Lungs were clear to auscultation bilaterally. She was able to lie supine without dyspnea for the physical examination. Airway examination was reassuring.

Given the unremarkable echocardiogram with normal biventricular function and inferior vena cava collapsibility, we opined that she was relatively intravascularly depleted from third spacing and interstitial edema. Combined spinal-epidural anesthesia was induced using hyperbaric 0.75% bupivacaine 1.2 mL, intrathecal morphine 150 µg, and intrathecal fentanyl 15 µg without activation of the epidural catheter. An IV coload of 500 mL crystalloid was administered. The neuraxial procedure was technically challenging due to anasarca obliterating landmarks. A T4 sensory level to pinprick was achieved bilaterally. Blood pressure was maintained in the normal range with phenylephrine infusion at 50 µg/min and intermittent boluses of phenylephrine and ephedrine. She was placed supine with left uterine displacement. Standard antibiotic prophylaxis was delivered consisting of cephazolin 2 g IV.

On delivery, the fetus was noted to be extremely hydropic, and neonatal resuscitation was immediately initiated. The placenta was grossly edematous and weighed 635 g (>90th percentile). The patient had resolution of external jugular and scalp vein distension within seconds of delivery, and edema had receded from the level of the lower thorax to her knees by the end of the procedure. She was given judicious IV fluids due to edema and anticipated intravascular shift in the postpartum period. She received a total of 600 mL of lactated Ringer's solution and 300 mL associated with antibiotic and postpartum oxytocin infusions. Estimated blood loss was 1000 mL, and urine output was 70 mL over 106 minutes operative time. Fetal resuscitation was pursued for 1 h and was notable for the following findings: umbilical artery blood gas: pH 7.26, $Paco_2$ 60, Pao_2 <30, bicarbonate 25. Unfortunately, fetal demise was declared at 1 h and 8 minutes after delivery despite aggressive resuscitative measures. The family declined fetal autopsy and further workup of the etiology of fetal hydrops. Blood culture was ultimately negative for bacterial growth and negative immunoglobulin G direct antiglobulin test.

She was monitored in the obstetric intensive care unit immediately postoperatively and transferred to a telemetry monitored bed on the postpartum ward with uneventful recovery. She received 2 doses of IV furosemide (total 20 mg) with improvement in oliguria and edema. She remained free of heart failure symptoms, and renal function as assessed by calculated glomerular filtration rate remained normal. Vital signs remained within normal limits without the development of hypertension. The patient was discharged in stable condition on postoperative day 2, and her shortness of breath and edema completely resolved by postoperative day 11.

Extensive laboratory tests were sent to determine the cause of fetal hydrops. Infectious workup was significant for a positive cytomegalovirus immunoglobulin G, negative cytomegalovirus immunoglobulin M, and high cytomegalovirus immunoglobulin G avidity, which is consistent with nonrecent cytomegalovirus exposure. Kleihauer-Betke test is a quantitative test to analyze the amount of fetal hemoglobin transferred to the mother's bloodstream, which showed no fetal-to-mother hemoglobin transfer. Thyroid function tests were within normal limits. Urine studies for preeclampsia were not obtained, because patient

remained normotensive. Cardiac operative report from her initial surgery was obtained, which revealed repair of 2 small atrial septal defects, closure of patent foramen ovale, and pulmonary valvotomy for pulmonic stenosis. Family history was significant for congenital heart disease. She denied any known consanguinity or known recessive genetic diseases in the family. As an infant, she was reportedly tested and negative for a hereditary condition causing her congenital heart disease. She denied using tobacco, alcohol, or illicit substances.

DISCUSSION

Mirror syndrome represents a rare constellation of findings, including fetal hydrops, maternal edema, and placental edema, with multiple possible causes. The initial case description was published by Ballantyne¹ in 1892 as a result of rhesus isoimmunization. It is also known as Ballantyne syndrome or triple edema due to the pathognomonic findings of maternal edema, fetal, and placental hydrops. A systematic review from 2010 found 56 case reports of Mirror syndrome²; 1 retrospective study from China estimates the rate of Mirror syndrome to be 0.015%.³ The syndrome typically presents with anasarca, proteinuria, and mild elevation in blood pressure. One case report described development of heart failure symptoms in a patient without a cardiac history in parallel with fetal hydrops.⁴ The condition can sometimes be confused with preeclampsia, although there are certain features that can help differentiate the etiologies of maternal edema⁵ (Table).

Anesthetic management of the patient with Mirror syndrome has been described, and, to our knowledge, ours is the first reported case that involved a comorbid diagnosis of unspecified congenital heart disease. Both vaginal and cesarean deliveries have been described for patients with Mirror syndrome at term or preterm gestation. Xu et al⁶ described general anesthesia for cesarean delivery for a woman with Mirror syndrome who also had pulmonary edema and Hemolysis, Elevated Liver Enzymes and Low Platelets Syndrome with a platelet count of $90 \times 10^9/L$. Her course was complicated by massive postpartum hemorrhage; the neonate was unable to be successfully resuscitated. Tayler and DeSimone⁷ discussed the management of a morbidly obese parturient with Mirror syndrome using a combined spinal-epidural technique. The maternal hospital course was complicated by postpartum cellulitis and discharge on hospital day 11; the neonate died on day 25. McCann et al⁸ described epidural labor analgesia in a case of labor induction and pregnancy termination for Mirror syndrome with a fetus of 21 weeks gestation. A nonviable fetus was delivered vaginally. In these cases, attention was paid to fluid management, consideration for preeclampsia spectrum disorders, and risk for pulmonary edema. Taken together, maternal outcomes may differ by anesthesia type, but it is not clear that anesthesia choice for cesarean delivery would have a significant impact on the neonatal outcome of Mirror syndrome in cases where the fetal risk is already high.

Although no definitive cause of Mirror syndrome has been discovered, the edematous placenta is suspected to play an inciting role in the development of maternal edema mediated through circulating angiogenic factors.^{9,10} Common immunologic causes of fetal hydrops leading to Mirror syndrome include severe fetal anemia due to rhesus isoimmunization and twin-twin transfusion. Nonimmunologic causes such as intrauterine infection, commonly parvovirus B19, and cytomegalovirus and fetal structural abnormalities such as aortic

stenosis and Ebstein's anomaly, alpha thalassemia, sacrococcygeal teratoma, and placental tumors¹¹⁻¹³ have been described. Traditionally, the condition is treated by reversing the underlying cause of fetal hydrops, such as intrauterine cordocentesis and transfusion for fetal anemia.¹⁴ Resolution of symptoms has been seen in cases of spontaneous or artificial feticide in Mirror syndrome due to twin-twin transfusion syndrome^{15,16} or fetoscopic photocoagulation of communicating placental vessels.¹⁷ Definitive treatment is delivery of the fetus and placenta. In the majority of cases, however, Mirror syndrome carries poor prognosis for the fetus, with an intrauterine death rate of 56%,² and maternal morbidity can be high secondary to pulmonary edema and renal failure.

In our patient, no definitive cause of fetal hydrops was elucidated. Fetal anemia could not be diagnosed due to inability to obtain middle cerebral artery Dopplers and lack of further laboratory studies after delivery due to parental refusal. Kleihauer-Betke test and maternal antibody screen also argued against isoimmunization cause of fetal hydrops. Serology for congenital infection was only significant for positive cytomegalovirus immunoglobulin G titers with high avidity and low immunoglobulin M titers, consistent with infection >3 months before presentation and therefore unlikely to be the cause of fetal abnormalities. Regardless of the cause of fetal hydrops in our patient, her clinical presentation of volume overload with an unclear history of congenital heart disease posed a diagnostic and therapeutic challenge for her intravascular volume status and anesthetic management of her cesarean delivery. Differential diagnoses of her edema initially included heart failure, preeclampsia, and Mirror syndrome. Preeclampsia was judged to be unlikely due to the combination of normotension, polyhydramnios, and large-for-gestational-age fetus. Her echocardiogram was functionally normal, arguing against heart failure as a cause of her edema. The echocardiogram had signs consistent with postsurgical changes, suggesting that she may have had a completely corrected congenital heart lesion. Given these findings (normal cardiac structure and function, nonsystemic infectious etiologies, and volume status assessment provided by the echocardiogram), we judged that she was an appropriate candidate for neuraxial anesthesia for her cesarean delivery. We elected to use crystalloid instead of colloid intraoperatively because crystalloid is no less effective than colloid in reducing the incidence of hypotension after spinal anesthesia for cesarean delivery, particularly when combined with vasopressors.¹⁸ There are additional concerns about nephrotoxicity associated with hydroxyethyl starch solutions, which we judged to be undesirable in a patient whose optimal renal function postoperatively would be important in addressing the generalized anasarca.¹⁹ Her symptoms dramatically improved immediately after delivery of the fetus, further supporting the diagnosis of Mirror syndrome.

Maintaining a broad differential diagnosis in a pregnant patient presenting with edema is important, and Mirror syndrome should be considered when coexisting fetal edema is present and other explanations are not sufficient. Anesthetic choice for the surgical management of a patient with Mirror syndrome depends on the urgency with which delivery must occur, maternal comorbidities, and the severity of symptoms. Despite a history of congenital heart disease, our patient had normal cardiac function based on echocardiogram and findings suggestive of bicuspid aortic valve and surgically corrected anomalies, as well as intravascular volume depletion despite overt edema. Awareness of her intravascular fluid status allowed us to proceed safely with thoughtful induction of neuraxial anesthesia and to

administer fluid to compensate for sympathectomy and blood loss without significant fear of cardiogenic shock and pulmonary edema. Because delivery is the definitive treatment for Mirror syndrome, it is prudent for the anesthesia team to seek information on fluid status and cardiac function in a patient with suspected Mirror syndrome undergoing urgent cesarean delivery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: Dr Lim is supported in part by the Department of Anesthesiology, University of Pittsburgh School of Medicine, and by an award from the National Institutes of Health Building Interdisciplinary Research Careers in Women's Health (K12HD043441).

REFERENCES

1. Ballantyne J The Disease and Deformities of the Fetus. Edinburgh, United Kingdom: Oliver & Boyd; 1892.
2. 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;27:191–203. [PubMed: 20357423]
3. Zhao Y, Liu G, Wang J, Yang J, Shen D, Zhang X. Mirror syndrome in a Chinese hospital: diverse causes and maternal fetal features. *J Matern Fetal Neonatal Med*. 2013;26:254–258. [PubMed: 23035798]
4. Li H, Gu WR. Mirror syndrome associated with heart failure in a pregnant woman: a case report. *Int J Clin Exp Med*. 2015;8:16132–16136. [PubMed: 26629125]
5. van Selm M, Kanhai HH, Gravenhorst JB. Maternal hydrops syndrome: a review. *Obstet Gynecol Surv*. 1991;46:785–788. [PubMed: 1780115]
6. Xu Z, Huan Y, Zhang Y, Liu Z. Anesthetic management of a parturient with mirror syndrome: a case report. *Int J Clin Exp Med*. 2015;8:14161–14165. [PubMed: 26550388]
7. Tayler E, DeSimone C. Anesthetic management of maternal Mirror syndrome. *Int J Obstet Anesth*. 2014;23:386–389. [PubMed: 25066819]
8. McCann SM, Emery SP, Vallejo MC. Anesthetic management of a parturient with fetal sacrococcygeal teratoma and mirror syndrome complicated by elevated hCG and subsequent hyperthyroidism. *J Clin Anesth*. 2009;21:521–524. [PubMed: 20006261]
9. Rana S, Venkatesha S, DePaepe M, Chien EK, Paglia M, Karumanchi SA. Cytomegalovirus-induced mirror syndrome associated with elevated levels of circulating antiangiogenic factors. *Obstet Gynecol*. 2007;109(2 pt 2):549–552. [PubMed: 17267891]
10. Stepan H, Faber R. Elevated sFlt1 level and preeclampsia with parvovirus-induced hydrops. *N Engl J Med*. 2006;354:1857–1858. [PubMed: 16641410]
11. Carbillon L, Oury JF, Guerin JM, Azancot A, Blot P. Clinical biological features of Ballantyne syndrome and the role of placental hydrops. *Obstet Gynecol Surv*. 1997;52:310–314. [PubMed: 9140132]
12. Chaoui R, Bollmann R, Hoffmann H, Zienert A, Bartho S. [Ebstein anomaly as a rare cause of a non-immunological fetal hydrops: prenatal diagnosis using Doppler echocardiography]. *Klin Padiatr*. 1990;202:173–175. [PubMed: 2355721]
13. Mizrahi-Arnaud A, Wilkins Haug L, Marshall A, Silva V. Maternal mirror syndrome after in utero aortic valve dilation. A case report. *Fetal Diagn Ther*. 2006;21:439–443. [PubMed: 16912494]
14. Valsky DV, Daum H, Yagel S. Reversal of mirror syndrome after prenatal treatment of Diamond-Blackfan anemia. *Prenat Diagn*. 2007;27:1161–1164. [PubMed: 17828794]

15. Chang YL, Chao AS, Hsu JJ, Chang SD, Soong YK. Selective fetocide reversed mirror syndrome in a dichorionic triplet pregnancy with severe twin-twin transfusion syndrome: a case report. *Fetal Diagn Ther.* 2007;22:428–430. [PubMed: 17652930]
16. Pirhonen JP, Hartgill TW. Spontaneous reversal of mirror syndrome in a twin pregnancy after a single fetal death. *Eur J Obstet Gynecol Reprod Biol.* 2004;116:106–107. [PubMed: 15294378]
17. Matsubara M, Nakata M, Murata S, Miwa I, Sumie M, Sugino N. Resolution of mirror syndrome after successful fetoscopic laser photocoagulation of communicating placental vessels in severe twin-twin transfusion syndrome. *Prenat Diagn.* 2008;28:1167–1168. [PubMed: 18925575]
18. Tawfik MM, Hayes SM, Jacoub FY, et al. Comparison between colloid preload and crystalloid co-load in cesarean section under spinal anesthesia: a randomized controlled trial. *Int J Obstet Anesth.* 2014;23:317–323. [PubMed: 25281437]
19. Mutter TC, Ruth CA, Dart AB. Hydroxyethyl starch (HES) versus other fluid therapies: effects on kidney function. *Cochrane Database Syst Rev.* 2013:CD007594. [PubMed: 23881659]

Figure 1. Fetal ultrasound images showing (A) thickened placenta (red triangles identify placental border) and (B) polyhydramnios (red arrow identifies expanse of amniotic fluid). Placental edema is a finding consistent with a diagnosis of Mirror syndrome.

Figure 2.

Fetal ultrasound images that assisted in diagnoses of fetal hydrops. Two compartments of fetal edema are required for the diagnosis of fetal hydrops. A, Fetal ultrasound showing fetal cranium with significant subcutaneous scalp edema. Red arrow identifies fetal epidermis. B, Fetal bilateral pleural effusions. Red triangles delineate borders of pleural effusions. C, Fetal face profile demonstrating significant subcutaneous edema.

Qualitative Comparison of Specific Features Differentiating Mirror Syndrome From Preeclampsia and Congestive Heart Failure

Table.

	Mirror Syndrome	Preeclampsia	Congestive Heart Failure
Maternal edema	Present	Present	Present
Hypertension	Absent or mild	Mild to severe	May be hypotensive
Proteinuria	Sometimes present	Almost always present	Usually absent
Amniotic fluid	Polyhydramnios	Oligohydramnios	Unaffected
Placenta size	Large	Usually small	Unaffected
Fetal size	Hydrops	Growth restriction	Unaffected
Hematocrit	Hemodilution	Hemoconcentration	Hemodilution
Serum uric acid	Sometimes elevated	Elevated	Sometimes elevated
Onset	116–34 wk	>20 wk	Any time