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Mirror syndrome in monochorionic diamniotic twins presenting as maternal hyponatremia: A case report

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ABSTRACT

This is a case report of a 39-year-old patient, G5P1031, with monochorionic diamniotic twins at 30 weeks and 1 day of gestation, who developed mirror syndrome without twin-to-twin transfusion syndrome (TTTS) with a unique presentation of maternal and neonatal hyponatremia. Coinciding with severe hyponatremia were maternal symptoms of edema, nausea and vomiting, hypoalbuminemia, elevated uric acid, as well as fetal selective growth restriction, polyhydramnios, umbilical artery absent end diastolic flow and prolonged bradycardia of twin B. Given the poor status of twin B and the risks to twin A, the patient underwent emergent cesarean delivery. Hyponatremia in all three patients resolved in the following 48–72 h. Mirror syndrome is associated with significant maternal and fetal morbidity and mortality. In this case, severe hyponatremia posed additional risks. Therefore, electrolyte monitoring should be considered in both mother and neonate(s).

1. Introduction

The association of maternal edema with fetal and placental hydrops due to rhesus isoimmunization was first described by John W. Ballantyne in 1892 [1]. This rare occurrence of "mirroring" of maternal and fetal pathology has since been described as Ballantyne's syndrome, pseudotoxemia, maternal hydrops syndrome, pregnancy toxemia, acute second-trimester gestosis, triple edema, or mirror syndrome [2,3]. In the 1970s, with advances in prenatal diagnosis and ultrasound, non-immunological, structural causes were established, including fetal supraventricular tachycardia, vertical cytomegalovirus (CMV) and parvovirus B19 infection, cardiac defects, sacrococcygeal teratoma, and twin-to-twin transfusion syndrome (TTTS) [4–6].

The incidence of mirror syndrome is unknown. A 2017 systematic review reports 113 cases in the literature [7]. Underdiagnosed and therefore underreported, mirror syndrome is thought to represent a form of preeclampsia, with edema occurring in approximately 90%, hypertension in 60%, and proteinuria in 40% of cases [3,8]. Usually manifesting between 16 and 34 weeks of gestation, additional maternal findings may include headache, visual disturbances, oliguria, elevated uric acid, liver function tests and creatinine levels, thrombocytopenia, anemia, and hemodilution [3,7,8].

The pathophysiology of mirror syndrome has not been completely established. Due to its similarities to preeclampsia, it has been proposed to involve a similar functional alteration in the placenta [9]. Therefore, distinguishing between these diseases poses a diagnostic dilemma. Presentation of mirror syndrome can include hypertension and proteinuria consistent with the diagnosis of preeclampsia in approximately 50% of cases. Unlike preeclampsia, mirror syndrome can present earlier in pregnancy, with absence of hyperreflexia, hemodilution and low serum albumin [3,7]. Fetal findings often include hydrops, placental edema, polyhydramnios, anomalies, organomegaly, tumors, and oligohydramnios [7,10]. Posing additional difficulty, this constellation of maternal and fetal findings may precede each other independently by 1–2 weeks. Therefore, the sequence of symptoms is not helpful in predicting prognosis [7].

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This is a case report of a monochorionic diamniotic twin gestation with the development of mirror syndrome without TTTS, with an unexpected complication of maternal and neonatal hyponatremia.

2. Case Presentation

A 39-year-old patient, G5P1031, was referred to the high-risk obstetric team for monochorionic diamniotic twins. This was an IVF pregnancy due to unexplained infertility with a single-embryo transfer. Obstetric history was significant for three unexplained first-trimester miscarriages and a full-term singleton vaginal delivery five years previously, complicated by gestational diabetes mellitus (GDM). The patient's past medical history was otherwise noncontributory and she had no other endocrine disorders.

First-trimester ultrasound showed normal nuchal translucency for both twin A and twin B. Follow-up ultrasounds at 16 and 18 weeks of gestation were within normal limits and revealed no evidence of discordant growth or TTTS. At 17 weeks of gestation, she was diagnosed with GDM, which was well controlled with only dietary modifications. Her blood pressures were normal during the antepartum period.

At 20 weeks of gestation, fetal echocardiograms were performed and were within normal limits. For the remainder of the pregnancy, ultrasound scans were performed every two weeks to assess fetal growth and TTTS screening. At 24 weeks and 5 days of gestation, she had a consultation with fetal surgery due to fetal weight discordance of 23%, with larger twin A, as well as polyhydramnios of twin B (maximum vertical pocket 8 cm). Amniotic fluid for twin A measured within normal limits. There was no other evidence of fetal compromise and both fetal bladders were visible and cycling. On consultation with fetal surgery, due to the presence of cycling bladders and normal Doppler evaluation, it was determined that there no evidence of TTTS or twin anemia polycythemia sequence (TAPS). As the diagnosis at this point was selective fetal growth restriction (FGR) type I with normal Doppler studies for both fetuses, the plan was for continued antenatal surveillance. The patient was offered amniocentesis with cytomegalovirus (CMV) screening, which she declined.

At 29 weeks and 5 days of gestation, the patient was sent from the fetal evaluation unit to labor and delivery because twin B had new-onset umbilical artery absent end diastolic flow and polyhydramnios with a maximum vertical pocket of 11 cm. The placenta appeared subjectively enlarged compared with prior exams. The patient had no obstetric or general complaints and her vital signs on presentation were within normal limits. She was admitted to antepartum for inpatient fetal monitoring. She was given intramuscular dexamethasone (4 doses of 6 mg) to accelerate fetal lung maturity. On hospital day 2, the patient had reactive non-stress tests (NST) and reassuring biophysical profiles. On hospital day 3, she completed the course of dexamethasone and the plan was for discharge. However, the fetuses had nonreactive NSTs, and biophysical profiles were completed. The biophysical profiles were again reassuring, but the decision was made to keep the patient overnight for continued monitoring and ultrasound to repeat umbilical artery Doppler assessment.

On hospital day 4, the patient reported feeling generally unwell, experiencing dizziness and nausea. She noted significant swelling of her vulva and bilateral lower extremities. Her blood pressure was 130 s/70s, heart rate in the 60s, and oxygen saturation was 99% on room air. She had one episode of emesis. Suspecting preeclampsia, a complete blood count, comprehensive metabolic panel, coagulation studies and urine protein to creatinine ratio were requested. The lab reported a critically low sodium level of 116 mmol/L. The remaining labs, including electrolytes and creatinine, were within normal limits. On clinical evaluation, she reported slight dizziness and weakness. Her mental status and physical examination were unremarkable. EKG was normal sinus rhythm. A repeat specimen was sent to confirm that the report of hyponatremia was not a lab error. The repeat sodium level was 118 mmol/L, and an urgent renal consultation and intensive care unit screen were requested. Urine sodium and potassium were within normal limits. Serum and urine osmolality were 252 and 137 mOSm/kg, respectively.

The patient was transferred to labor and delivery for cardiac and fetal heart rate monitoring. Due to the inability to obtain fetal heart rates using the external fetal monitor, bedside ultrasound revealed twin A had a heart rate in the 140 s and twin B persistently in the 40s over several minutes. Given the poor status of twin B despite maternal resuscitation efforts and the subsequent risks to twin A, the decision was made to proceed for emergent cesarean delivery under general anesthesia. Given her severe hyponatremia, the plan for intraoperative management included conservative use of crystalloid (0.9% normal saline). If the case was prolonged, the plan from the anesthetic standpoint was intraoperative monitoring of sodium with corrective measures as appropriate.

The cesarean section was uncomplicated with an estimated blood loss of 800 cc and 750 cc of crystalloid given. The patient was transferred to the intensive care unit for further monitoring with a target sodium correction of 4–6 mmol/L in 24 h. Within 12 h of delivery, the maternal hyponatremia had self-corrected from 112 to 125 mmol/L. She received 2 μg of desmopressin and 1.5 L of dextrose 5% in water infusion over 1 h to prevent further over-correction, and was placed on 1 L/day fluid restriction afterward. Her sodium level continued to self-correct and her clinical status returned to normal prior to discharge (Table 1). Postoperative chest X-ray was normal with no evidence of pulmonary edema. Her transthoracic echocardiogram was normal with an ejection fraction of 65%. Gross evaluation of the placenta was notable for an edematous appearance and subjective enlargement based on gestational age. The placental pathology and histology were unremarkable.

Twin A was a male infant, delivered vertex with a loose nuchal cord. Apgar scores for twin A were 8 and 8, and birth weight was 1435 g. Twin B was also a male infant, delivered by breech presentation, with Apgar scores of 2 and 5, and birth weight of 1250 g. Twin B was intubated and taken to the NICU. Twin A cord gases were arterial pH 7.35 with base excess 2.7 mEq/L. Twin B cord gases were arterial pH 6.84 with base excess 19.5 mEq/L. Twin A and twin B had hyponatremia of 121 and 111 mmol/L, respectively. Twin B received hypertonic saline and sodium bicarbonate, with resolution of hyponatremia within 72 h. Twin A autocorrected over the next 48 h.

The patient was discharged 5 days postpartum and twin A at 51 days of life and twin B at 69 days of life.

3. Discussion

This case report is one of few in the literature describing mirror syndrome in a patient with monochorionic diamniotic twins without TTTS. To the authors' knowledge, this is the first reported case of the syndrome presenting with maternal and neonatal hyponatremia. After performing a literature search for “mirror syndrome pregnancy” and “mirror syndrome hyponatremia” on PubMed, there were no cases found that associate mirror syndrome with maternal and neonatal hyponatremia. A single published case report from Norway describes mirror syndrome in a dichorionic twin pregnancy at 28 weeks and 1 day of gestation, with a mildly low serum of sodium 132 mmol/L [11]. In our case, coinciding with hyponatremia were maternal symptoms of significant vulvar and lower extremity edema, nausea and vomiting, hypoalbuminemia, elevated uric acid, as well as polyhydramnios, umbilical artery absent end diastolic flow and bradycardia of twin B.

Mirror syndrome can manifest in several ways. Although this case fit the common maternal features with simultaneous fetal findings in a monochorionic twin gestation, hyponatremia was unexpected. Although not reported in cases of mirror syndrome, several reports in the literature note hyponatremia associated with preeclampsia. A descriptive study of 277 singletons and 55 twin gestations with preeclampsia noted hyponatremia in 32 (9.7%) of patients [12]. Hyponatremia was independently associated with preeclampsia with severe features (OR 2.3, $p = 0.004$), and occurred more frequently in twin gestations ($p = 0.001$)

Table 1
Maternal lab values throughout her hospital stay.

				DAY			
	Baseline	1	4	5	6	7	8
		(admission)	(delivery)				(discharge)
Hematocrit (34–47%)	36.2	35.7	35.5	30.9	33.8	31.3	
Platelet (150–450 K/uL)	178	179	203	150	171	190	
Sodium (135–145 mmol/L)	133		116, 118	125	129	135	135
Potassium (3.5–5.2 mmol/L)	4.3		4	4	4.9	4.2	4.3
Chloride (96–108 mEq/L)	106		89	97	100	103	103
Creatinine (0.5–1.1 mg/dL)	0.71		0.62	0.52	0.54	0.52	0.57
AST (<36 U/L)	14		36, 29	24		30	
ALT (<46 U/L)	17		40, 50	44		43	
Uric acid (2.5–6.0 mg/dL)			7.6				
Albumin (3.5–5.0 g/dL)	3.7		2.5	1.7		2.1	

and in patients who presented with edema ($p < 0.001$) [12]. There are several additional case reports of severe maternal hyponatremia due to preeclampsia in singleton and twin gestations, often with resultant fetal hyponatremia [13–16].

Severe hyponatremia (<120 mmol/L) can lead to convulsions, coma, and can be fatal in up to 50% of cases. Convulsions due to hyponatremia may be mistaken for eclamptic seizures, thus delaying diagnosis and management. Moreover, hyponatremia adds an additional seizure risk in combination with preeclampsia [14]. Rapid sodium replacement is also dangerous, potentially leading to pontine demyelination and quadriplegia [14,15]. Moreover, fetal sodium levels equilibrate with maternal levels, which can lead to fetal jaundice, tachypnea, and seizures [15].

The physiology of hyponatremia in pregnancy is not entirely understood. Proposed mechanisms include inappropriate secretion of vasopressin (SIADH) and raised renal sensitivity to normal arginine vasopressin levels [13]. Via a "reset osmostat" phenomenon, pregnancy normally causes release of ADH at lower thresholds, thereby reducing serum osmolality by 6-10 mmol/L as well as serum sodium levels, with a level of 130 mmol/L acceptable in pregnancy [12,17].

Hyponatremia is classified as hypovolemic (decreased total body water or deficit of extracellular sodium), normovolemic (normal or slight excess of total body water), or hypervolemic (excess of extracellular sodium or larger excess of total body water). Hyponatremia with hypovolemia can be due to renal or non-renal causes. Renal causes include mineralocorticoid deficiency, sodium-losing renal disorders and diuretic excess, and are associated with a urine sodium concentration of >20 mmol/L. Non-renal causes are associated with urine sodium concentration of <10 mmol/L and include profuse vomiting, prolonged diarrhea, extensive burns, and excessive sweating. Hyponatremia with normovolemia is associated with urine sodium >20 mmol/L. Causes include glucocorticoid deficiency, hypothyroidism, SIADH, and inappropriate use of intravenous fluids (e.g. 5% dextrose). Hyponatremia with hypervolemia can be due to renal causes where urine sodium is greater than 20 mmol/L and include acute or chronic renal failure. Non-renal causes are associated with urine sodium concentration of <10 mmol/L and include cardiac failure, cirrhosis, nephrotic syndrome, and inappropriate intravenous fluids (e.g. normal saline). Certain drugs, such as tricyclic antidepressants, opiates, dopamine antagonists, diuretics, selective serotonin re-uptake inhibitors, and chemotherapeutic agents have also been reported to cause hyponatremia [16,17].

This case showed mirror syndrome complicated by severe hyponatremia in a patient with normal serum glucose and electrolytes, normal serum creatinine, and absence of proteinuria. Also notable was the patient's extensive peripheral edema. Her vomiting was limited to two episodes, and she did not receive intravenous fluids until her cesarean delivery, in which 750 cc of crystalloid was given. Besides antenatal corticosteroids for fetal lung maturity, she was not on any other medications. Although the exact cause remains unclear, this patient may have had hyponatremia with hypervolemia due to mirror syndrome and elevated ADH which resolved rapidly after delivery. This hypothesis is based on the fact that 30 min after delivery, her urine osmolarity was 137 mosm/kg, which dropped to 90 mosm/kg around five hours later with sodium auto-correcting to 125 mmol/L. The patient was noted to have dilute urine output (300-700 cc/h) until desmopressin was given to prevent over-correction. Serum osmolarity was 252mosm/kg immediately after surgery.

Twin B presented with serum sodium of 111 mmol/L and was treated with hypertonic saline. The baby's serum sodium corrected quickly, which may indicate an SIADH process similar to the mother. Twin A had presenting sodium of 121 mmol/L, which auto-corrected over 2 days. Although this may indicate SIADH process similar to twin B and the mother, the higher level of sodium may also point towards a lowering of serum sodium due to the shared circulation of twin B and twin A.

4. Conclusion

To the authors' knowledge, maternal and subsequent neonatal hyponatremia is not a common clinical presentation of mirror syndrome in monochorionic diamniotic twins. Upon performing a literature search for "mirror syndrome pregnancy" on PubMed, there were no cases in the literature of mirror syndrome that presented with maternal and neonatal hyponatremia. The number of reported cases of mirror syndrome are limited overall, and the pathophysiology is poorly understood. As it is associated with increased maternal and fetal morbidity and mortality, a high index of suspicion is warranted. Electrolyte monitoring should be considered in both mother and neonate(s).

Contributors

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Conflicts of interest statement

The authors declare that they have no conflict of interest regarding

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