

Mirror Syndrome associated with Patau Syndrome: A Case Report

Síndrome de espelho associada a uma síndrome de Patau: um relato de caso

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Abstract

Keywords

- ▶ pregnancy
- ▶ hydrops fetalis
- ▶ pulmonary edema
- ▶ trisomy 13 syndrome

Mirror syndrome is an unusual pathological condition in which maternal edema in pregnancy is seen in association with severe fetal and/or placental hydrops. The disease can be life-threatening for both the mother and the fetus. The pathogenesis is poorly understood, and may be confused with preeclampsia, even though distinguishing features can be identified. We report a rare case of mirror syndrome with maternal pulmonary edema associated with fetal hydrops due to Patau syndrome.

Resumo

Descritores

- ▶ gravidez
- ▶ hidropsia fetal
- ▶ edema pulmonar
- ▶ síndrome de trissomia 13

A síndrome de espelho é uma patologia invulgar na qual o edema materno é observado em associação com hidropsia fetal e/ou placentária graves. Esta doença pode ser fatal para a mãe e para o feto. A sua patogênese é mal compreendida, e pode ser confundida com pré-eclâmpsia, mesmo com características distintivas identificadas. Relatamos um caso raro de síndrome de espelho com edema pulmonar materno associado a hidropsia fetal devido a síndrome de Patau.

Introduction

In 1892, Ballantyne was the first to put forward a syndrome characterized by maternal edema in pregnancy associated with fetal and placental hydrops, due to rhesus (Rh) isoimmunization.¹ Afterwards, O'Driscoll² named this disease mirror syndrome, since the maternal edema reflects the fetal and placental hydrops, like a mirror. As it is extremely uncommon and frequently underdiagnosed, the incidence of mirror syndrome is unknown, with less than 100 cases reported worldwide.^{1,3}

Mirror syndrome is associated with both immune and non-immune causes of fetal hydrops, such as Rh isoimmunization, viral infections, fetal or placental malformations, twin-to-twin transfusion syndrome, and fetal arrhythmia.⁴ The pathogenesis and pathophysiology remain incompletely understood, with features similar to those of preeclampsia, which may hamper the diagnosis and misdirect decision-making.^{4,5}

In the following case report, we present a case of mirror syndrome associated with Patau syndrome.

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Case Description

A 29-year-old black primigravida was transferred to our department at 26 weeks of gestation with fetal hydrops.

The patient had a history of malaria in childhood and a family history of thromboembolic events. Her blood type was B Rh-positive, with a negative antibody screen.

The pregnancy was followed since the first trimester (with normal evolution), and the patient was medicated with folic acid and iodine. In the routine analyses, the pregnant woman had a negative infectious screening. The fetal ultrasound examination at 13 weeks revealed nuchal translucency (NT) < 95% and a ductus venosus pulsatility index of 95% for the gestational age. The patient had a 0.98 multiple of median (MoM) NT, with 1.18 MoM pregnancy-associated plasma protein-A (PAPP-A) and 2.12 MoM free β -human chorionic gonadotrophin (β -hCG), which could have led to a false negative first trimester combined screening of aneuploidies (trisomy 21 = 1:2337, trisomy 13 and 18 = < 1:100000). At 22 weeks, the fetal ultrasound was apparently normal, and no echocardiography was performed.

At 26 weeks of gestational age, the patient presented to the emergency department with nausea, vomiting, epistaxis, weight gain (9 Kg/1 week, totalizing 76 Kg) and edema, with the progression occurring over 48 hours. Her blood pressure was 170/120 mm Hg, and the urine dipstick test showed intense proteinuria. Ultrasound examination revealed fetal hydrops.

Intravenous infusions of labetalol, dexamethasone and magnesium sulfate were initiated, and the patient was transferred to our department, a tertiary center with differentiated perinatal support. Upon admission, the patient's blood pressure was 136/74 mm Hg, with normal diuresis (300cc/8h); therefore, labetalol and magnesium sulfate were suspended. An analytical study showed a level of hemoglobin of 11.9 mg/dL, hematocrit 35.5%, platelet count of $190 \times 10^9/L$, protein to creatinine ratio in urine of 1.4, a level of uric acid of 8.7 mmol/L, a level of human chorionic gonadotrophin (hCG) of 1,091.939 mIU/mL, and normal hepatic function tests. The infectious screening was also negative (HIV, hepatitis B, A and C: negative; parvovirus, herpes simplex virus, Epstein Barr virus and cytomegalovirus: immune).

The ultrasound examination confirmed fetal hydrops with subcutaneous and facial edema, pericardial effusion, hydrothorax, severe ascites and placental edema (thickness of 7.2 cm). The amniotic fluid index was decreased (deepest pocket of 3 cm), as well as the active fetal movements (absence of suckling and swallowing). A detailed fetal morphology scan revealed a hyperechoic intestine. The fetal echocardiography showed cardiomegaly with interventricular communication and apparently dysmorphic and insufficient tricuspid valve. Subsequently, an amniocentesis was performed to investigate cytogenetic anomalies.

On the third day of hospitalization, the patient presented with tachypnea, with increased generalized edema, decreased diuresis (620cc/24h) and normal blood pressure; subsequently, the administration of furosemide and enoxaparin was initiated. A laboratory analysis revealed anemia

(hemoglobin 9.6 mg/dL, hematocrit 28.2%) and hypoproteinemia (total protein 4.8 g/dL, albumin 2.3 g/dL), with normal hepatic and renal functions. By this time, the postulated diagnosis was mirror syndrome.

After the elucidation of both maternal and fetal prognoses (early gestational age versus worsening maternal condition), a medical interruption of the pregnancy was proposed, which was accepted by the patient. After performing the feticide (intracardiac injection of potassium chloride), the delivery protocol was performed with misoprostol, and finalized with a stillbirth. The external habit of the fetus was very macerated, with hydrops, hypotelorism, medium face and nose hypoplasia, long philtrum, small mouth with fine lips and upper lip in cupid's bow, high palate, and postaxial polydactyly of hands and feet.

After delivery, the patient suffered a heavy blood loss due to uterine atony, which reverted with uterine massage and oxytocin infusion; two units of blood transfusion were needed. Four hours after the delivery, the patient began presenting with dyspnea, high blood pressure, sleepiness and prostration, despite the medical treatment with furosemide, labetalol and magnesium sulfate. Thus, with mirror syndrome complicated with acute lung edema and hypertension, the patient was transferred to the intensive care department. In that unit, the medical treatment was optimized, with progressive recovery.

Four days later, the patient returned to our department, with no complaints, weighing 10 Kg less than when she was hospitalized, and medicated with losartan and captopril.

Afterwards, the maternal course was favorable: the mirror syndrome resolved on the fourth day, and the patient was discharged seven days after the delivery.

The quantitative fluorescence-polymerase chain reaction (QF-PCR) analysis of the amniotic fluid revealed Trisomy 13/Patau syndrome.

The placental histology demonstrated a large placenta for the gestational age due to edema, immaturity and exuberant hematopoiesis.

An autopsy of the fetus confirmed the hydrops, with prominent subcutaneous tissue edema, pleural and ascitic hemeroserous effusions and multiple internal anomalies. A cardiac examination confirmed the anomalies previously suspected. Abnormal azygos vein, macroscopic hepatic calcifications and accessory spleen were also detected. All these features can be integrated in Patau syndrome.

Discussion

Mirror syndrome is extremely rare in the clinical practice, easily underdiagnosed, and associated with many causes. Furthermore, this disease is associated with increased maternal morbidity and mortality.

The case reported in the present study was an unusual form of mirror syndrome. Indeed, in the literature, including the largest series of cases published in 2010, there is no case related to Patau syndrome.¹ In our case, the etiology of the mirror syndrome was associated with Patau syndrome, which was undetected both in the first trimester biochemical

screening of aneuploidies and in the morphological obstetrical ultrasound performed at 22 weeks of gestation.

The clinical manifestations of this disease are complex, including weight gain and edema, accompanied by high blood pressure, with or without proteinuria, oliguria, tachycardia and tachypnea.^{1,4} Severe maternal complications, including acute respiratory failure due to pulmonary edema, happened in our case, and it occurs in 21.4% of cases.¹ Laboratory analyses usually show signs of hemodilution with mild anemia, hypoalbuminemia, hyperuricemia, and higher human chorionic gonadotrophin (hCG) levels.⁶ Therefore, this disease can be easily confused with preeclampsia, making it difficult to diagnose and manage.⁵ Nevertheless, the different hallmark is hemodilution, instead of hemoconcentration, which is present in preeclampsia.⁴ Additionally, liver function tests and the platelet count usually remain unaffected in mirror syndrome.⁷

The similarity between the two diseases is also seen in the pathogenesis, as in mirror syndrome there is an anti-angiogenic state similar to what is seen in preeclampsia, which resolves after fetal delivery.⁸ The pathogenesis and pathophysiology of mirror syndrome remain misunderstood, but it is thought that placenta-derived anti-angiogenic factors may be involved.^{1,4} Llurba et al⁸ suggest that there is a direct link between the trophoblastic damage caused by the placental edema and an imbalance in angiogenic factors in the maternal circulation that ultimately cause endothelial dysfunction and the clinical manifestations of mirror syndrome. Furthermore, hCG elevation could be used as a clinical marker for placental disturbance.⁶

According to literature reports, the gestational age for the onset of this syndrome ranges from 16 to 34 weeks; our case occurred at an early gestational age (26 weeks).¹

Mirror syndrome can be reversible when the underlying factors are identified and modified.^{4,9} If correction of the underlying fetal abnormality is not possible (as in our case), the consensual treatment is to deliver the hydropic fetus and placenta, with improvement of the maternal condition shortly thereafter. In the meantime, supportive therapy for maternal stability, with diuretics and antihypertensive therapy, is crucial.^{4,9} The average time of maternal recovery described in the literature is 8.9 days, with a 35.7% rate of intrauterine deaths and stillbirths; in our case, this was observed in four days.¹

Conclusion

In conclusion, this case of mirror syndrome associated with Patau syndrome demonstrates how fetal structural malformations can lead to fetal hydrops, being mirrored by the

maternal symptoms. Physicians should be attentive for this diagnosis, due to its poor prognosis, with potential fetal mortality and high maternal morbidity. Therefore, timely treatment in the form of delivery of the fetus and placenta is essential to achieve the best outcome. Further experimental and clinical studies are necessary to clarify the pathophysiology of mirror syndrome, namely how fetal hydrops leads to placental edema.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

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