J Med Sci 2019;39(6):284-288
DOI:10.4103/jmedsci.jmedsci_25_19

CASE REPORT

A Very Rare Case of Mirror Syndrome Presenting with Concurrent Posterior Reversible Encephalopathy Syndrome

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The objective is to present clinical and neuroimaging findings of a very rare patient diagnosed with mirror syndrome and associated posterior reversible encephalopathy syndrome (PRES). A 19-year-old Syrian, primigravida in the 38th week of gestation was admitted with a severe headache and consciousness impairment developing within a 1-day period. At admission, she was confused and noncooperative, and she developed two consecutive seizures. After prompt cesarean section, the patient recovered completely within 3 days. However, the fetus was hydropic and had deep anemia. The fetus died 5 h after birth due to cardiopulmonary insufficiency. A retrospective evaluation yielded the diagnosis of mirror syndrome. On the other hand, further investigations due to the neurological manifestations of the mother yielded the diagnosis of PRES in association with mirror syndrome. Mirror syndrome should be kept in mind as an important differential diagnosis in circumstances of preeclampsia-like presentations. In addition, to our knowledge, this case also constitutes the first report illustrating a patient with mirror syndrome and concurrent PRES.

Key words: Mirror syndrome, neuroimaging, pathogenesis, posterior reversible encephalopathy syndrome

INTRODUCTION

Hypertensive disorders of pregnancy contribute notably to maternal morbidity and mortality. Eclampsia is one of the hypertensive gestational diseases, characterized by seizures. Major maternal complications include placental abruption, aspiration pneumonia, neurological deficit, pulmonary edema, cardiopulmonary arrest, and acute renal failure. On the other hand, Ballantyne syndrome (mirror syndrome) is a scarcely diagnosed condition, which constitutes a crucial differential diagnosis of eclampsia/preeclampsia and can be life-threatening for both fetus and mother.[1] It is characterized by various fetal and placental manifestations including feta-maternal edema, preeclampsia, and polyhydramnios; and "triple edema" has been particularly emphasized for the diagnosis.[2] The diagnosis of mirror syndrome can be difficult as it may be confused with preeclampsia, although distinguishing features can be recognized.[3] It can cause a very high fetal and maternal morbidity and mortality; therefore, early diagnosis and intervention are critical.[4] On the other hand, underlying pathogenesis has not been fully illuminated. In this report, we describe a pregnant woman who finally received the diagnosis of mirror syndrome associated with fetal anemia and thrombocytopenia. In addition, the neurological manifestations of concurrent posterior reversible encephalopathy syndrome (PRES) will be illustrated in detailed through follow-up neuroimaging findings as well as electroencephalography (EEG) recordings. Based on this first reported case and literature review, underlying pathogenesis of Ballantyne syndrome as well as PRES will be discussed.

CASE REPORT

A 19-year-old Syrian primigravida was in the 38th week of gestation. She was brought to the hospital by her relatives due to a severe headache and progressive consciousness impairment developing within a 1-day period. At admission, she was confused and noncooperative. Initial blood pressure was 200/120 mmHg. Soon after her admission, the patient

Received: February 09, 2019; Revised: April 22, 2019; Accepted: May 28, 2019
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How to cite this article: Onder H, Comba C. A very rare case of mirror syndrome presenting with concurrent posterior reversible encephalopathy syndrome. J Med Sci 2019;39:284-8.

had two consecutive, generalized seizures. With a provisional diagnosis of eclampsia, a 4.5 g intravenous (IV) magnesium sulfate and iv diazepam were administered which provided cessation of seizures. Soon after, she was urgently intubated. Transabdominal ultrasonography revealed fetal skin edema, minimal fetal ascites, placental abruption, and prolonged fetal bradycardia. Hence, the cesarean section (C/S, using abdominal incision) was performed 30 min after admission. The fetus (female) was born weighing 3000 g, 50 cm in length. Apgar score was evaluated as 3 at 1 min and 5 at 5 min after birth. The fetus was mild-moderate hydropic and widespread petechial lesions were observed [Figure 1]. Maternal blood examinations of liver function tests and platelet values were within the normal range. Therefore, hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome was not considered. However, other laboratory examinations revealed a mild anemia suggesting to be caused by hemodilution (Hgb: 8.3 g/dL, hematocrit [HCT]: 26.5%, platelet: 150.000/μL, Na: 132 mmol/L [135–145], alanine transaminase: 9 U/L [N], aspartate aminotransferase: 23 U/L [N], albumin: 2.3 g/dL [3.5–5.2], and urea: 33 mg/dL [N]). The fetal umbilical cord blood investigations revealed acidosis (pH: 6.57, base excess – 25.7 mmol/L), deep anemia (hemoglobin [Hb]: 4.4 g/dL), low platelet count (27000/μL), and leukocytosis (33,000/μL; monocyte: 26% [0–12.5], lymphocyte: 43% [N], neutrophil: 27% [N]). The fetus died 5 h after birth due to cardiopulmonary insufficiency. Taken together (triple edema, deep anemia of fetus, maternal normal liver functions, and platelet count), the diagnosis of mirror syndrome was established and mother was transferred to the intensive care unit after C/S. Maintenance therapy of magnesium sulfate infusion (2 g/h) was continued. Albumin and calcium replacements, cabergoline, and antihypertensive treatments (amlodipine 2 g × 10 g) were administered. Besides, oral levetiracetam (2 mg × 500 mg) was added to the treatment. For further investigation and monitoring of the confusional state and seizures (at admission), a routine EEG was performed 1 day after C/S which revealed severe, generalized widespread slowing in the background activity [Figure 2a]. Concurrent cranial computed tomography showed diffuse cortical edema. Cranial magnetic resonance imaging (MRI) showed bilateral widespread cortical edema in the frontal-parietal and temporal lobes [Figure 3a]. Based on the clinical (altered consciousness, seizures, and acute hypertension) and radiological findings, an associated diagnosis of PRES was considered. In the subsequent period, resolution in hypertensive measurements was achieved, and antihypertensive medications were gradually tapered. She was evaluated as totally oriented and cooperative in the following course (3 days after C/S). Cranial MRI recorded 2 weeks later showed nearly totally resolution of cortical edema [Figure 3b]. Concurrently performed EEG showed normalization of the background activity [Figure 2b].

Figure 1: Moderate hydropic fetus

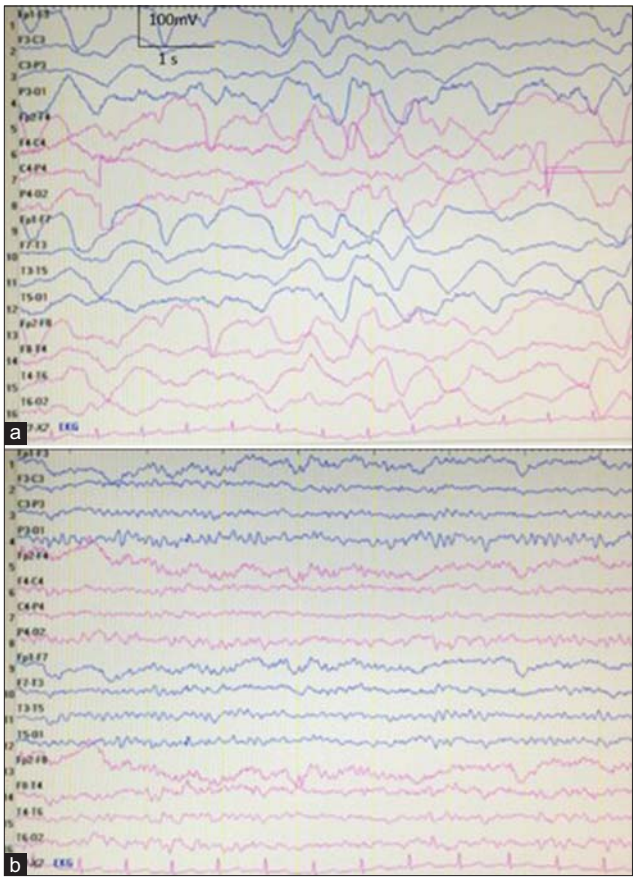

Figure 2: (a) First electroencephalography showing generalized severe slowing of the background. (b) Electroencephalography performed 2 weeks later showed recovery of the background activity to 7–8 Hz

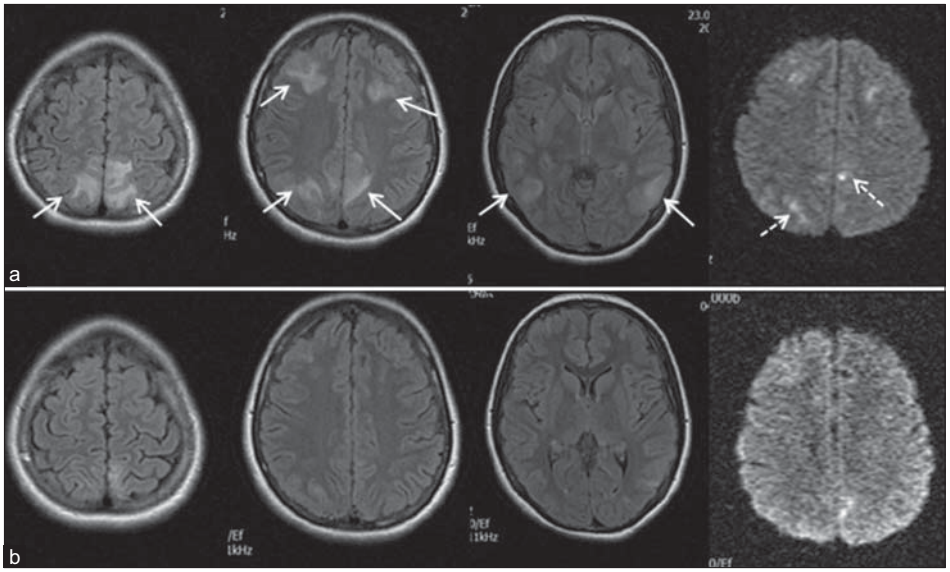

Figure 3: (a) Brain magnetic resonance imaging showing bilateral frontal, parietal, and temporal cortical vasogenic edema (arrows) and diffusion restricted sites (intermittent arrows). (b) Second magnetic resonance imaging (performed 12 days later) showing nearly totally recovery of lesions

DISCUSSION

Mirror syndrome is an extremely rare disorder of pregnancy which presents with symptoms and findings resembling eclampsia. It was first introduced by Ballantyne in 1892[5] and fewer than 100 cases have been reported since then.[6] He had emphasized the association of maternal edema with fetal and placental hydrops at that time. Albeit some suggested mechanisms, the underlying pathophysiology of mirror syndrome still remains to be elucidated. In the study by Wu *et al*., focusing on the data of a large patient population, etiology of mirror syndrome was classified as Bart's hydrops fetalis, fetal complicated congenital cardiac anomalies, and unknown etiology.[4] All 12 cases were diagnosed in the third trimester. Headaches and visual disturbances, as well as laboratory measurements of proteinuria, hypoproteinemia, elevated liver enzyme, thrombocytopenia, HELLP syndrome, acute pulmonary edema, placental abruption, amniotic fluid embolism, and disseminated intravascular coagulation, have been reported to be involved in the manifestations of mirror syndrome. Hypertension and abnormal laboratory findings had normalized within 5–7 days after delivery. However, pointing out the importance of identification of this entity, perinatal mortality was reported to be 100%.[4] In a crucial report of retrospective analyses of the patients with mirror syndrome, rhesus isoimmunization, twin-twin transfusion syndrome, viral infection, and fetal malformation were found as the etiological agents.[2] Unfortunately, the underlying etiology in our case could not be determined. However, in our case, fetal hydrops was not severe, and the prominent findings were deep anemia, thrombocytopenia, and leukocytosis (monocytosis) supporting the sight of an underlying viral infection. However, our etiological diagnosis was a clinical one without laboratory confirmation. On the other hand, we associated the clinical picture of the mother, including mirror syndrome, placental abruption, elevated blood pressure, and PRES with deep fetal anemia and mild-moderate fetal hydrops. The main treatment of mirror syndrome is the delivery of the fetus.[4] Additional treatments include magnesium sulfate and symptomatic treatments such as antihypertensive drugs, anticonvulsive therapy. In accordance with this, after C/S, severe hypertension and encephalopathy recovered totally within the following 3 days.

In our case, normal liver functions and platelet counts supported the diagnosis of mirror syndrome; but more importantly, fetal blood investigations revealed deep anemia and thrombocytopenia and fetus was evaluated as hydropic. Another point emphasized in the differentiation from preeclampsia is the hemodilution in mirror syndrome, whereas in preeclampsia hemoconcentration has rather been reported to occur.[7] This also supported the diagnosis of mirror syndrome in our case (Hb: 8.3 g/dL; HCT: 26.5 %).

Remarkably, further investigations for seizures and mild encephalopathy yielded the diagnosis of PRES. PRES can be defined as neurological manifestations such as a headache, visual disturbances, and consciousness alterations associated with MRI findings of T2 hyperintensity in the occipital-parietal lobes.[8] Although the exact pathophysiology of PRES remains unknown, there are two hypotheses emphasized: First is the "vasogenic theory" pointing out

the role of hypertension exceeding the cerebrovascular autoregulation limits leading to vasodilation and disruption of the blood–brain barrier.[9] On the other hand, the second view of endothelial theory primarily emphasizes the endothelial damage as the initial factor leading to the blood–brain barrier disruption.[10] In addition, the function of immune response and some specific cytokines such as tumor necrosis factor alpha, vascular endothelial growth factor have been hypothesized to be involved in the pathophysiology of PRES.[11] PRES has been reported most commonly in association with acute hypertension, renal disease, sepsis, exposure to immunosuppressants as well as preeclampsia or eclampsia.[12-15] However, to our knowledge, mirror syndrome in association with PRES has not been reported before. Hence, this case constitutes the first report of a patient with mirror syndrome and concurrent PRES, providing potentially substantial perspectives regarding the pathophysiology of mirror syndrome as well as PRES.

For example, in mirror syndrome, fetal and placental hydrops has been accounted as the inducer agent of pathological circles.[3] Considering the concurrent occurrence of PRES, we can suppose a similar pathophysiological pathway, which functions both in the fetus and pregnant through crossing the placenta. This view may support the role of cytokines, which can cross placenta through circulation, as a crucial pathway among mechanisms of mirror syndrome and PRES. On the other hand, this report, illustrating the neurological involvement of PRES in Mirror syndrome as in preeclampsia/eclampsia, may also add another support to the consideration of classifying mirror syndrome under the head of preeclampsia, as suggested previously similarly.[16]

In our opinion, mirror syndrome should be kept in mind as an important differential diagnosis in circumstances of preeclampsia-like presentations.[17] Although prognosis has been reported to alter according to the etiology, generally the prognosis is poor[17] and reversal of maternal symptoms can be achieved by the urgent removal of placenta, either by the termination of pregnancy or by delivery.[16] In addition, this report adds substantial data constituting the first report illustrating PRES in mirror syndrome in the literature. Future studies of large case series reporting these rare co-occurrences will add to understand the unsolved aspects of the underlying pathogenesis of these entities.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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