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Case Report Open Access

Cerebral Vasospasm in Cortical Blindness Associated with Preeclamsia/Eclampsia Syndrome

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Abstract

Background: Preeclampsia/eclampsia syndrome (Pe/ES) is a frequent complication during pregnancy. Neurologic or visual disturbances associated with Pe/ES are acute and severe. The women with cerebrovascular syndromes (CVS) are at increased risk of cerebrovascular complications that may lead to permanent sequelae and death.

Case Reports: We describe the clinical course of three obstetric patients with Pe/ES complicated by CVS and cortical blindness. Posterior reversible encephalopathy syndrome (PRES) was seen in the three patients. One patient had the coexistence of PRES and reversible cerebral vasoconstriction syndrome. Transcranial Doppler (TCD) confirmed cerebral vasospasm in two patients. Follow-up with TCD allowed sequential assessments of the evolution of cerebral vasospasm.

Conclusion: The variability of cerebral hemodynamics in Pe/ES could be the cause of diverse clinical and radiological expressions of these CVS. Cortical blindness is a manifestation of CVS associated to Pe/ES. PRES-cortical blindness associated with preeclampsia without seizures is an entity with severe neurologic dysfunction.

Keywords: Cerebral vasospasm; Cortical blindness; Preeclampsia/Eclampsia; Transcranial doppler

Introduction

About 7% of pregnant women attending health facilities in Africa, Asia, Latin America and the Middle East are at risk of potentially life-threatening disorders and 1% develop severe maternal outcome (maternal death or maternal near miss). In these women, post-partum hemorrhage and preeclampsia/eclampsia syndrome (Pe/ES) are the two most frequent obstetric complications in 26.7% and 25.9% respectively. The risk of maternal death is four times more frequent in women with preeclampsia and increasing up to 42 times more in women with eclampsia, when compared with women without these conditions. Although less frequent in organ dysfunction related to pregnancy, neurological dysfunction makes up 11.3% of women with a severe maternal outcome [1-3]. The cerebral circulation has a central role in some acute neurologic manifestations in the Pe/ES and require prompt investigation between cerebrovascular syndromes (CVS), cerebrovascular complications and central nervous system pathological conditions. The CVS include reversible posterior encephalopathy syndrome (PRES), reversible cerebral vasoconstriction syndrome (RCVS) and coexistence of both (PRES/RCVS). The diagnosis and treatment of these acute clinical and radiological syndromes may be difficult to establish.

Eclamptic seizures are preceded by a variety of acute visual symptoms up to 45% of cases. The women with persistent visual symptoms may present an ophthalmic entity that requires specific therapy. The ophthalmic entities associated with Pe/ES are reversible cortical blindness, serous retinal detachment, Purtscher-like retinopathy, central retinal vein occlusions, and vitreous hemorrhages. The incidence of reversible cortical blindness in eclampsia has been found in 15% of women [4-9].

There are a few case reports about association of CVS and cortical blindness with Pe/ES, and cerebral hemodynamic follow up. The present report describes the characteristics of three patients with Pe/ES complicated by CVS and cortical blindness, identifies the cerebral hemodynamic changes in Pe/ES with neurologic dysfunction by CVS.

Materials and Methods

Over a 4-year period from January 2010 to December 2013, 110 obstetric patients were admitted to the medical and surgical adult intensive care unit of the Hospital Civil de Guadalajara "Fray Antonio Alcalde" (tertiary care referral and teaching hospital in western México). Pe/ES was an indication for admission in 43 patients. Of these, three patients with Pe/ES presented CVS and cortical blindness.

The Pe/ES was defined according to the criteria of the American College of Obstetricians and Gynecologists. Preeclampsia was defined as a persistent systolic blood pressure (BP) of 140 mm Hg or higher, or a diastolic BP of 90 mmHg or higher after 20 weeks of gestation in a woman with previously normal BP, as well as new-onset proteinuria. In the absence of proteinuria, preeclampsia was defined as a new-onset hypertension with a new onset of any of the following: thrombocytopenia, impaired liver function, renal insufficiency, pulmonary edema and cerebral or visual disturbances.

Preeclampsia with severe features was defined as preeclampsia along with any of these findings: systolic BP of 160 mm Hg o higher, or a diastolic BP of 110 mm Hg or higher, thrombocytopenia, impaired liver function, renal insufficiency, pulmonary edema, cerebral or visual disturbances and persistent right upper quadrant or epigastric severe pain.

Eclampsia was defined as the presence of new-onset grand mal seizures in a woman with preeclampsia [10].

PRES was defined as a clinical acute neurological syndrome including headache, altered mental function, seizures, loss of vision and focal neurological signs associated with lesions of vasogenic edema by neuroimaging. The reversibility of vasogenic edema is required on follow-up imaging [11,12].

RCVS was defined as a clinical acute neurological syndrome with neuroradiological diagnostic criteria including multifocal segmental cerebral artery vasoconstriction assessed by magnetic resonance angiography, computed tomography (CT) angiography, or conventional angiography with angiographically proven reversible vasoconstriction [13-15].

Coexistence of PRES/RCVS included the diagnostic criteria of PRES and RCVS.

Cortical blindness was defined as a loss of vision associated with an intact pathway from the eye to the lateral geniculate bodies, and therefore, the pupillary light responses and ocular motility remain intact [5].

Cerebral hemodynamics monitoring was determined by transcranial Doppler (TCD) ultrasound (Sonara/tek TCD system) with a pulsed 2 MHz probe. The mean cerebral blood flow velocities (CBFV mean) of the anterior cerebral artery (ACA), middle cerebral artery (MCA), posterior cerebral artery (PCA), extracranial internal carotid artery (ecICA), basilar artery (BA) and vertebral artery (VA) of both hemispheres were measured by TCD. The normal range of CBFV mean was considered according to guidelines for TCD: ACA of 30 to 80 cm/s, MCA of 30 to 80 cm/s, PCA of 20 to 60 cm/s, ecICA of 20 to 70 cm/s, BA of 20 to 60 cm/s and VA of 20 to 50 cm/s [16,17]. The pulsatility index and Lindegaard ratio were calculated automatically by TCD ultrasound.

The MCA vasospasm criteria for subarachnoid hemorrhage were implemented. The TCD criteria for cerebral vasospasm were defined by CBFV mean in MCA >120 cm/s and Lindegaard ratio (CBFV mean of MCA divided by CBFV mean of ecICA on the same side). A Lindegaard ratio below 3 indicating no severe vasospasm and for the vertebrobasilar system was of >80 cm/s [18-21].

The severity of vasospasm was considered in two grades: moderate-grade (CBFV mean in MCA >120 cm/sec) and high-grade (velocities of 200 to 250 cm/s in the MCA) [18,22]. Normal reference values for the pulsatility indices were 0.7-0.3 [23].

In all patients the first examination with TCD was performed within 24 h of the patient´s was transfer to the intensive care unit (day 0). It was repeated in all patients to monitor vasospasm until they were discharged from the hospital and also repeated outside of the hospital until normalization of CBFV mean in MCA. A trained investigator performed all TCD measurements. Mean arterial blood pressure (MABP) was assessed before each TCD examination. Neurologic and ophthalmologic consultants assessed the patients.

Case Reports

Patient 1

A 29-year-old woman at 24 weeks of gestation was admitted to the hospital with severe features of preeclampsia. Her pregnancy was unremarkable until 9 days earlier when she started with an intermittent severe headache and phosphenes. She received hydralazine and alpha methyldopa in a primary health care unit 3 days prior for an arterial BP of 140/90 mm Hg.

Upon admission to the emergency department, she reported worsening of her headache, as well as nausea and dizziness. She had severe hypertension with BP of 190/110 mm Hg (MABP of 137 mm Hg) and bilateral pedal edema. Hydralazine and magnesium (Mg) sulfate were begun immediately. The fetal evaluation with Doppler ultrasonography showed a live product with a partial placental abruption, and dexamethasone was indicated for fetal pulmonary immaturity. Her blood cell count, liver function and coagulation tests were within normal limits. A urinalysis revealed proteinuria and granular casts.

Her obstetric history was significant for: gravida 4, caesarean 1 and abortion 2 without history of hypertension or headache in previous pregnancies.

On her day 1 of admission, she started with vaginal bleeding by placental abruption. Her placental separation was 50%, which led to premature interruption of her pregnancy through an urgent caesarean delivery. A subarachnoid block was performed with bupivacaine, after that, she presented hypotension and response to crystalloid, colloid and ephedrine. She delivered a live female child, weighing 980 g that died on day 7 secondary to prematurity complications.

Fifteen hours after caesarean, the patient complained of acute bilateral blindness. Her BP at that time was 140/100 mm Hg (MABP of 113 mm Hg) and an urgent CT scan was performed which showed cerebral edema. The patient was transferred to the intensive care unit. At the time of admission, her BP was 145/89 mm Hg (MABP of 108 mm Hg); she had generalized edema and a normal neurologic examination. Her pupils were isochoric, dilated, poorly reacting to light and visual fields revealed no light perception. In addition, generalized arteriolar narrowing and retinal flame hemorrhages were found by indirect ophthalmoscopy examination.

Initial TCD showed vasospasm at the beginning of visual symptoms and intravenous nimodipine was begun. The CBFV mean in MCA-right/left (R/L) were 104/195 cm/s, ACA-R/L of 64/89 cm/s, PCA-R/L of 48/77 cm/s, ecICA-R/L 49/42 cm/s, BA of 60 cm/s and VA-R/L of 59/75 cm/s. The MCA pulsatility index-R/L was 0.61/0.56 and Lindegaard ratio-R/L of 2.1/4. Twelve hours after treatment her vision was better. The CBFV mean decreased on day 1, but still remained with vasospasm. Visual symptoms remitted on day 2, but there was an increase in CBFV mean in MCA-R/L of 251/181 cm/sec with pulsatility index-R/L of 0.56/0.84 and Lindegaard ratio-R/L of 8.4/5.4 on day 4, related with an increase in BP of 160/100 mm Hg (MABP of 120 mmHg) on this day, without visual disturbance. The patient regained vision completely before her BP and vasospasm returned to normal.

Magnetic resonance imaging (MRI) was performed after 48 h with high-signal lesions on white matter in both posterior parietal lobe (Figure 1), and evidence of segmental, multifocal vasoconstriction of the cerebral arteries by magnetic resonance angiography. A diagnosis

of PRES/RCVS with vasospasm and cortical blindness in severe preeclampsia was made.

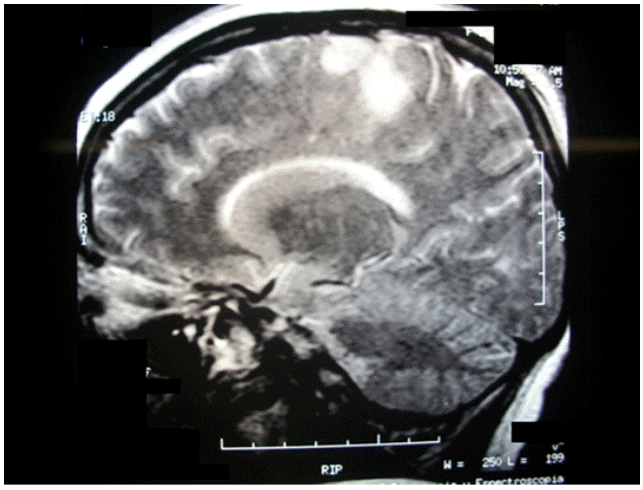
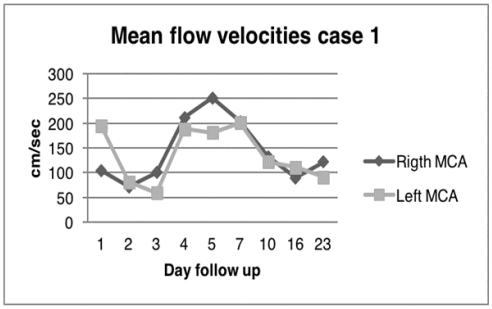


Figure 1: High-signal lesions on white matter in both posterior parietal lobe.

She was transferred back to the maternity ward after 3 days in the intensive care unit. The findings of TCD on day 3 indicated vasospasm and antihypertensive treatment including metoprolol, captopril, nifedipine and prazocin. Oral nimodipine was indicated by 3 weeks once intravenous infusion was stopped on day 2 after the vasospasm diagnosis.

A follow-up ophthalmologic examination was performed 6 days after admission and complemented with a normal fluorangiography. Fundus examination revealed retinal exudates, flame hemorrages and mild tortousity of the vessels. Her visual acuity was 20/20 and 20/13 in the right and left eyes respectively. Anterior segment findings were unremarkable.

The patient was discharged from the hospital on day 10 with instructions to follow up at the intensive care unit for a TCD check (Graph 1). Antihypertensive drugs were stopped gradually on follow up visits and she did not need any medication on third week after being discharged. The nimodipine was stopped in the follow-up visit in the third week.



Graph 1: TCD check.

Patient 2

A 18-year-old primigravida woman at 41 weeks of gestation was admitted to the emergency department for eclampsia. She was transferred from another hospital because she had been experiencing by 4 h hypertension after presenting a severe bitemporal and occipital headache, blurred vision, tinnitus, and vomiting. On admission, the patient had simple partial seizures of the lower jaw and right upper limb, severe hypertension with BP of 220/120 mmHg (MABP of 153 mmHg), edema of the lower extremities and 2 uterine contractions every 10 min. Hydralazine, phenytoin and Mg sulfate were begun immediately. Her laboratory values revealed 17.2 g/dL of haemoglobin (Hb), liver function tests with 1.5 mg/dL of total bilirubin, 305 IU/L of alkaline phosphatase and 314 IU/L of lactic acid dehydrogenase. Serum potassium was 2.7 mmol/L and coagulation tests were within normal limits. A urinalysis revealed proteinuria.

The patient´s prenatal course had been complicated at 25 weeks by placental abruption requiring hospitalization for 3 days. She was on no medications.

An urgent caesarean under general anesthesia was performed on the day of admission. The course of anesthesia and surgery was uneventful, except by placental abruption of a 25% rear face. A viable female infant was delivered and the patient was transferred to the intensive care unit. At the time of admission, she was intubated with PaO2 of 57 mmHg; lactate of 2.5 mmol/ L and her BP was 161/122 mm Hg (MABP of 135 mmHg). We begun with the following antihypertensive treatment: hydralazine, methyldopa and nifedipine. Her pupils were isochoric and reactive to light with a normal fundus examination. Sedation and tracheal intubation were stopped after 24 h. After she recovered from sedation, she complained of blurred vision, dizziness and her BP was 159/104 mm Hg (MABP of 122 mm Hg) with hyperreflexic limbs. Her Hb was 14.2 g/dL. The findings of TCD were CBFV mean normal and MCA pulsatility index-R/L of 1.15/0.83.

On day 2, she was alert, non-oriented, with increased right-side hyperreflexia and an urgent CT scan was unremarkable. Her BP was 174/90 mmHg (MABP of 118 mmHg) and other antihypertensive drugs were started: nitroglycerin, prazosin, metoprolol and captopril; a blood cell count was 11.8 g/dL of Hb. The TCD with CBFV mean in MCA-R/L of 114/103 cm/s, ACA-R/L of 82/41 cm/s, PCA-R/L of 33/64 cm/s, ecICA-R/L 47/39 cm/s, BA of 23 cm/s and VA-R/L of 59/40 cm/s; the MCA pulsatility index-R/L of 1.58/0.59 and Lindegaard ratio-R/L of 2.4/2.6.

On day 3, she complained of worsening blurred vision until present bilateral blindness, intermittent severe headache and tinnitus. She had hyperreflexic limbs and her BP was 137/86 mm Hg (MABP of 103 mm Hg). The TCD with evidence of vasospasm with right predominance: CBFV mean in MCA-R/L of 228/151 cm/s, ACA-R/L of 130/63 cm/s and PCA-R of 127 cm/s. Furthermore, with MCA pulsatility index-R/L of 0.38/0.49 and Lindegaard ratio-R/L of 4/3. Oral administration of nimodipine was started immediately. A MRI showed lesions of increased signal intensity on T2 and Flair in cortico-subcortical right occipital lobe (Figure 2). A diagnosis of PRES with vasospasm and cortical blindness in eclampsia was made.

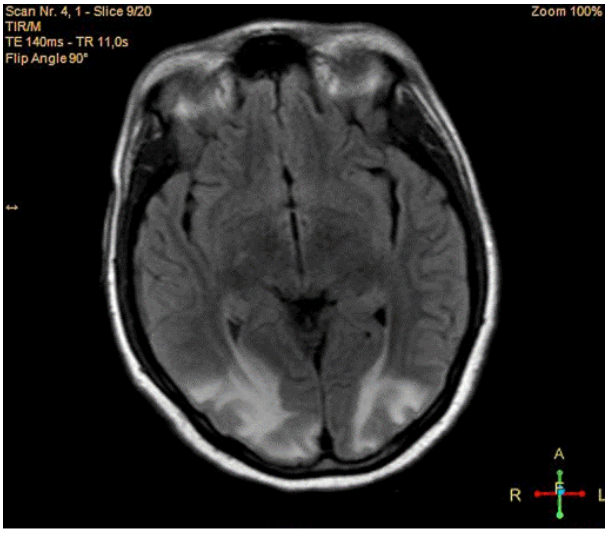
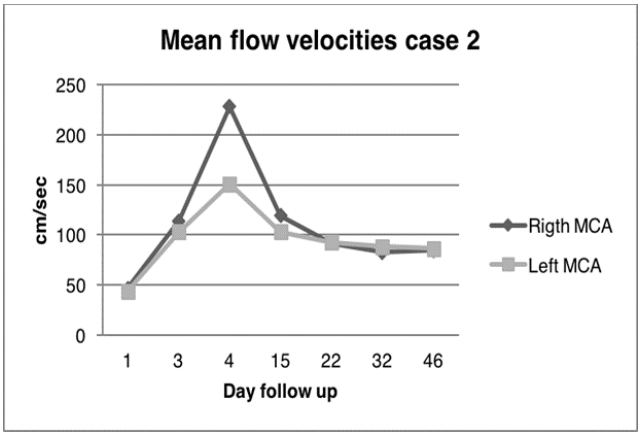


Figure 2: A diagnosis of PRES with vasospasm and cortical blindness in eclampsia.

On day 4, she experienced complete visual recovery before her BP and CBFV mean returned to normal, and she was transferred back to the maternity ward after 5 days in the intensive care unit with antihypertensive treatment. On day 8, proteins in the 24 h urine collection were within normal range. She was discharged at home 9 days postpartum with metoprolol, captopril, prazosin, nimodipine and phenytoin. Nimodipine was continued for 3 weeks. A follow-up TCD was performed after admission to intensive care unit (Graph 2). After normalization of the CBFV mean, the MCA pulsatility index-R/L was 0.72/0.82.



Graph 2: TCD was performed after admission to intensive care unit.

Patient 3

A 20-year-old primigravida woman at 29 weeks of gestation without prenatal care during her pregnancy was admitted to the hospital for eclampsia. She was transferred from a primary health care unit due to headache, followed by 4 episodes of seizures and severe hypertension with BP of 190/150 mm Hg (MABP of 163 mm Hg). She was treated with hydralazine, diazepam and phenytoin.

Upon admission to the emergency department, she was conscious and oriented, with generalized edema, increased osteotendinous reflexes, BP of 148/90 mm Hg (MABP of 109 mm Hg) and fetal heart rate of 80 beats/min. During the monitoring, she presented with tonic-clonic generalized seizures once more and phenytoin and Mg sulfate were begun immediately. Laboratory values revealed impaired renal function with blood creatinine of 1.95 mg/dL. Liver function tests with 149 IU/L alkaline phosphatase, 174 IU/L alanine aminotransferase, 313 IU/L aspartate aminotransferase, 670 IU/L lactic acid dehydrogenase and 1.7 g/dL albumin. Her Hb was 17.6 g/dL and serum electrolytes and coagulation tests were within normal limits. A urinalysis revealed proteinuria.

Caesarean under general anesthesia was performed due to fetal bradycardia and eclampsia. The course of anesthesia and surgery was unremarkable except that her BP reached levels of 107/68 mm Hg (MABP of 81 mm Hg). A live male weighing 1310 g was delivered and the patient was transferred to the intensive care unit. At the time of admission, she was intubated with BP of 155/93 mm Hg (MABP of 114 mm Hg), heart rate of 113 beats/min, pupils isochoric with low reacting to light, increased osteotendinous reflexes and her Hb was 15.3 g/dL.

Antihypertensive treatment included captopril, metoprolol and nifedipine. Sedation and tracheal intubation were stopped after 9 h. After extubation, she complained of reduced visual acuity and could only see white color.

On day 2, she had bilateral blindness, bradilalia, left hemiparesis and right gaze deviation. Visual fields revealed no light perception although the ophthalmoscopy was normal. Her BP at that time was 151/119 mm Hg (MABP of 130 mm Hg). Laboratory values revealed a creatinine of 2 mg/dL, serum potassium of 6.6 mmol/ L and Hb of 12.5 g/dL. A CT scan was performed with unremarkable results.

Initial TCD was normal and a MRI performed at 24 h of bilateral blindness, showed lesions of increased signal intensity on T2 and Flair on white matter cortico-subcortical in both frontal, parietal and occipital lobes (Figure 3). A diagnosis of PRES with cortical blindness in eclampsia was made. On day 3, the vision improved but the hemiparesis persisted. On day 4, she regained vision completely with improvement of hemiparesis. On day 5, she reached normal blood creatinine levels and was transferred back to the maternity ward. On day 9, urinary protein after 24 h collection was 2.5 g.

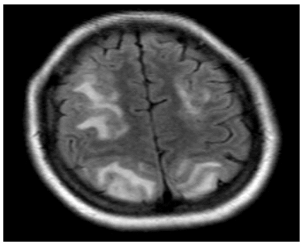


Figure 3: Flair on white matter cortico-subcortical in both frontal, parietal and occipital lobes.

The patient was discharged from hospital on day 11 with captopril and nifedipine. No follow-up was performed with TCD.

Characteristic of the three patients

None of these patients presented in their past history a diagnosis of neurologic or ophthalmologic disease, chronic hypertension, drug abuse or use of vasoactive medications.

Hypertensive crisis was detected in patients 1 and 2 at admission in the emergency department. The patient 3 was transferred from a primary health care unit after treatment of hypertensive crisis. Neurologic and visual disturbances had acute presentation in all patients.

On the time of first assessment with TCD, the patients had received Mg sulfate and antihypertensive treatment. The TCD showed vasospasm in two patients and was confirmed by magnetic resonance angiography in one of them. The patients with vasospasm were treated with nimodipine, one received initial intravenous infusion followed by oral administration and the other patient received only oral administration.

The cortical blindness was presented in the postpartum period in all patients. We observed the relationship between lowering MABP and CBFV mean in MCA when they had cortical blindness. The time of presentation was in the patient 1, on day 0 with MABP of 113 mm Hg. The patient 2 on day 3 had a MABP of 103 mm Hg and the patient 3 on day 2 had a MABP of 114 mm Hg.

Discussion

The heterogeneity of the clinical manifestations for the diagnosis of CVS, cerebrovascular complications and central nervous system pathological conditions is a challenge in Pe/ES. The CVS associated with Pe/ES include PRES (also called reversible posterior leukoencephalopathy syndrome, reversible posterior cerebral edema syndrome or reversible posterior encephalopathy syndrome), RCVS (also called benign postpartum angiopathy/Call-Fleming syndrome, postpartum cerebral angiopathy or reversible cerebral vasoconstriction syndrome) and the coexistence of PRES/RCVS. PRES is among the most frequent conditions associated with Pe/ES and occurs during the puerperium, rather than during pregnancy. Pregnancy itself may not be a predisposing factor of PRES [11,24,25].

Medical conditions described for PRES were excluded in the 3 patients.

In PRES associated with eclampsia, headache is the most common presenting symptom in 87.2% of women followed by altered metal status in 51.1% and visual disturbance in 34% [26]. Headache and visual disturbances were present in the 3 patients, and a focal neurologic deficit was observed in eclamptic women. A possible relationship between focal or generalized seizures could be vasogenic edema distribution. Although, the vasogenic edema seems to be focally enhanced in the posterior circulation, it affects all basal arteries and is identified in multiple areas of the brain. There is evidence that the Capillary density increases during pregnancy and contribute to the susceptibility of hypertension índuced vasogenic edema increasing the potential sites of blood-brain barrier disruption [27].

The incidence of abnormal findings by neuroimaging is unknown. In some case series, radiologic changes of PRES associated with eclampsia using MRI are of 97.9 to 100% [26,28-30]. MRI documents a transition between reversible vasogenic edema to irreversible cerebral ischemia and infarction [31]. Considering these findings, we support the hypothesis that PRES is the primary central nervous system injury in most patients with eclampsia. In patients 2 and 3 with eclampsia, MRI showed lesions of PRES. However, we observed PRES-cortical blindness associated with preeclampsia without seizures in the patient 1.

This finding demonstrated that cortical blindness is a manifestation of PRES associated with severe preeclampsia.

Puerperium is a precipitating factor of RCVS in up to 9% of women, others precipitating factors include the peridural injection of anesthetics associated with epinephrine and bromocriptine to inhibit lactation [13,32]. Vasoconstriction can be symptomatic, but also can persist after resolution of symptoms [33]. Cerebral angiography showed diffuse vasospasm of large-and medium-caliber arteries with occlusions of some terminal branches [34,35]. The severity of the vasospasm is determined by degree of vessel constriction and this variability results in diverse clinical and radiological expressions, in different patients as well as different territories of the same patient (36). TCD and transcranial color Doppler have been used for the assessment and follow-up of cerebral vasospasm in RCVS [13,37-40].

The incidence of coexistence of PRES/RCVS in Pe/ES is unknown. Cerebral vasoconstriction occurs in patients with PRES and vasogenic edema can occur in patients with RCVS [13,38,40]. In patient 1, vasospasm was identified by TCD at beginning of acute bilateral blindness and lesions of PRES with RCVS was seen in 48 h, when the patient regained vision completely before her BP and CBFV mean in MCA returned to normal. This patient was considered with two precipitating factors associated to RCVS, preeclampsia and exposure to drugs. She received ephedrine by hypotension after subarachnoid block.

Interestingly, we observed in cerebral hemodynamics of patient 2, progressive changes in CBFV mean in MCA up to vasospasm. These changes were classified into 4 patterns. The first pattern was a normal CBFV mean and increase pulsatility index; second pattern was an increase in both CBFV mean and pulsatility index; third pattern was with vasospasm and low pulsatility index and the fourth pattern of resolution was a gradual decreased of CBFV mean and increase of pulsatility index. We considered that the first pattern was affected by the hemoconcentration. On admission, the patient was volume depleted and part of her treatment included hemodilution. The hematocrit changes correlated with CBFV mean changes in the Pe/ES [41].

Other factors could be implicated directly with this increased in CBFV mean, like the intensity and duration of BP elevations, distribution of vasoconstriction and hemoconcentration. In follow-up with TCD, vasospasm was evident without clinical manifestations but with therapeutic normalization of the BP. It's difficult to determine how long these cerebral hemodynamic changes persist after postpartum. CBFV mean are normalized between 6 and 22 days after MABP has returned to normal [40,41]. In patient 2, CBF V mean took more time to return to normal range.

Critical levels of CBFV mean in patients with vasospasm should be avoided. The CBFV mean reaches maximum values a few days after delivery [41]. In patient 1, 251 cm/sec and patient 2, 228 cm/sec were the highest CBFV mean that were reached in MCA. In spite of both patients receiving antihypertensive drugs and nimodipine. The CBFV mean in MCA of 200 to 250 cm/sec are well tolerated in most patients

with subarachnoid hemorrhage, depending upon the extension of the spasm as well as other factors, such as the arterial and intracranial pressure. However, these velocities are potentially dangerous because they herald a reduction in cerebral blood flow [18]. CBFV mean in MCA of 380 cm/s were associated with ischemic lesions and petechial hemorrhage in the occipital cortex of a woman with cortical blindness and preeclampsia [42].

Several studies related with cerebral hemodynamics have been conducted in women with Pe/ES in order to determine the neuropathophysiology mechanism of their clinical manifestations. Diastolic BP>100 mmHg is associated with a significant increase in CBFV mean [40,43]. Similarly, MABP has been related with the degree of hyperperfusion. The degree of hyperperfusion depends on the maximal rise in MABP and correlates with the severity of clinical presentation [41].

Upon admission to the emergency department, only the patient 2 had MABP of 153 mmHg with simple partial seizures. However, the patient 3 had MABP of 163 mmHg with generalized seizures before to be transferred from a primary health care unit. Preeclamptic women had significantly higher cerebral perfusion pressure, a pattern of high average speed, significantly lower pulsatility index and resistance indices, and abnormal cerebrovascular autoregulation compared to normotensive pregnant women [44-50]. Preeclampsia does not induce greater side-to-side differences in CBFV mean or pulsatility index in the MCA distribution compared with normotensive women (47). Nevertheless, we found relevant differences between right and left CBFV mean MCA in patient 1, the vasogenic edema distribution and the degree of vasoconstriction could have direct association with these differences.

The severity of vasospasm could be followed by cerebrovascular complications. Postpartum period is associated with high risk of cerebral infarction and hemorrhage, with relative risks of 8.7 and 28.3 respectively. Pe/ES has been identified in cerebral venous thrombosis (9.6%), ischaemic stroke (36%) and cerebral hemorrhage (57.5%). Cerebral hemorrhage had the highest death rate of 15% [51,52]. CVS associated with Pe/ES can progress to cerebrovascular complications that may lead to permanent sequelae and death. Case reports of CVS associated with Pe/ES and cerebrovascular complications include: PRES with ischemic lesions, cerebral infarction, subarachnoid hemorrhage and hematoma [53-57]. RCVS with ischemic lesions and cerebral infarction [36,58,59]. While the coexistence of PRES/RCVS with transient splenial lesion, cerebral infarct, cerebral hemorrhage and subarachnoid hemorrhage [14,35,60-62].

The cortical blindness is an acute and dramatic complication of Pe/ES. Other authors have reported CVS with cortical blindness: PRES-cortical blindness associated with eclampsia [63-68]. PRES-cortical blindness associated with preeclampsia without seizures [54-57]. RCVS-cortical blindness associated with preeclampsia [36,59] and the coexistence of PRES/RCVS-cortical blindness associated with eclampsia [37]. Cortical blindness can be the primary clinical manifestation and be preceded seizures [9,65-67]. The mechanism is unclear whether it results from vasogenic edema or vasospasm and ischemic injury, TCD had demonstrated findings of vasospasm in temporary blindness associated with preeclampsia. In women with cortical blindness and preeclampsia, CBFV mean returned to normal within 2 weeks [42]. We suggest that pathophysiology of cortical blindness could be the same as CVS. Cortical blindness is a complication associated with PRES, RCVS, coexistence of PRES/RCVS and cerebrovascular complications. Blindness may be due to lesions at any site along the visual pathway, but the majority of case reports indicate lesions at the occipital cortex. Another presentation of bilateral blindness with agnosia of the visual deficit associated with PRES is Anton´s syndrome, denial of blindness. The finding of gaze palsies in the patient 3, indicated a low midbrain/high pontine lesion [65]. Cortical blindness is usually reversible. However, visual loss by infarcts may be permanent [66-75]. We do not have an explanation for the cortical blindness remission before resolution of vasospasm in patient 1 and 2. Treatment of cortical blindness in the setting of Pe/ES requires control of BP and observation [9].

Initial goal-directed strategy combined prompt symptomatic treatment and control of the causative factor [24]. Rapid control of seizures and BP are necessary to prevent cerebral damage. The iatrogenic lowering of MABP (<80 mm Hg) below the level necessary to maintain adequate cerebral perfusion pressure may worsen the brain damage in eclamptic patients [76]. There is little information about the effect of antihypertensive drugs on CBFV mean in Pe/ES. The lowering of MABP increased the CBFV mean in patients 1 and 2; it is possible that the vasospasm was in response to lowering MABP. Patients received different kind of antihypertensive drugs for BP control, changes may vary depending on what antihypertensive drugs are used. The reduction in BP results in a concomitant reduction in cerebral perfusion pressure; labetalol reduced cerebral perfusion pressure without adversely affecting CBFV mean [77]. Cerebral perfusion pressure in women with preeclampsia is elevated even after adequate treatment of elevated BP with methyldopa and nifedipine, the elevated cerebral perfusion pressure was also accompanied by an increase in CBFV mean in MCA and cerebral flow index [46].

Prophylaxis with Mg sulfate reduces the risk of eclampsia. Although, we know that Mg sulfate is better than nimodipine to prevent seizures in women with preeclampsia, we switched to nimodipine because the persistence of vasospasm determined by TCD [78-80]. In an effort to improve the symptoms, Mg sulfate infused over 6 days has been used in cortical blindness associated to preeclampsia [36,74].

Some limitations need to be considered in this study. First, we did not obtain MRI of lesion reversibility. Although PRES associated with Pe/ES shows maximal reversibility of the brain stem lesions on follow-up imaging [31,81], adverse sequelae after Pe/ES with imaging presence of cerebral white matter lesions have been reported on long-term follow-up [82]. In addition, RCVS in three-month follow-up angiograms demonstrate complete resolution of vasoconstriction [15,31]. Second, we adopted the sonographic criteria for vasospasm, from studies of subarachnoid hemorrhage and we do not know the grade of CBFV mean in MCA correlated to vasospasm in CVS associated with Pe/ES. Third, at the time of TCD the patients had been receiving Mg sulfate and antihypertensive treatment, meaning that the cerebral hemodynamics might have been altered. Fourth, patient 3 was not followed-up with TCD and we could not observe the cerebral hemodynamics in this patient.

Conclusion

PRES-cortical blindness associated with preeclampsia without seizures is an entity with severe neurologic dysfunction. PRES and RCVS are reported as unique and different entities, we considered that PRES and RCVS associated with Pe/ES are part the same condition with sequential events, but also can coexist. The diagnosis of patients with neurologic dysfunction depends on the time of evolution of CVS,

and the time that neuroimaging studies are carried out. We support the use of magnetic resonance angiography and TCD together in the evaluation of these patients, as they are complementary studies. Cerebral hemodynamic changes in Pe/ES with neurologic dysfunction by CVS must be monitored by TCD to decrease the risk of cerebrovascular complications. In our opinion, we suggest that the level of CBFV mean in MCA by TCD could be classified in four patterns of presentation:

Pattern I. Normal CBFV mean.

Pattern II. Increase in CBFV mean.

Pattern III. Vasospasm.

Pattern IV. Vasospasm with gradual decreased of CBFV mean.

When both TCD and angiographic studies are used, pattern II, could be associated with or without vasoconstriction. However, different conditions should be taken into account in these patterns (the presence of hypertensive crisis and the decrease in MABP, degree of hemoconcentration and antihypertensive drugs used). The variability of cerebral hemodynamics in Pe/ES could be the cause of diverse clinical and radiological expressions of these CVS. Cortical blindness is a manifestation of CVS associated to Pe/ES.

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