An intensive care approach to posterior reversible encephalopathy syndrome (PRES): An analysis of 7 cases

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Abstract

Objective: The aim of this study was to retrospectively evaluate the intensive care unit treatments applied to obstetrics patients with a diagnosis of posterior reversible encephalopathy syndrome (PRES).

Material and Methods: The cases of 7 pregnant patients who had been diagnosed with PRES between July 2011 and July 2013 were retrospectively reviewed. The patients’ clinical data, brain magnetic resonance imaging (MRI) images before and after treatment, and neuropsychological tests were evaluated.

Results: Five out of 7 patients had eclampsia, 1 patient had severe preeclampsia, and 1 patient developed HELLP syndrome secondary to PRES. Calcium channel blockers and β-blockers were used as antihypertensive treatment. All patients were treated with parenteral magnesium sulfate. In addition, sodium thiopental was given to control sedation and convulsions in all patients except 1. The neurological and radiological findings of all cases treated in the intensive care unit improved.

Conclusion: Posterior reversible encephalopathy syndrome is a clinical condition with a multifactorial etiology and can result in different clinical findings. Radiological imaging techniques can be used for the diagnosis of PRES. Pregnancy and the postpartum period often lead to this syndrome. In some cases, PRES can cause irreversible neurological deficits or death. For patients with severe radiological findings, early diagnosis and thiopental infusion, in addition to treatment with antihypertensive agents and magnesium sulfate, may lead to quicker and more effective recovery from clinical manifestations. We suggest supplementation of standard treatment with early thiopental infusion. (J Turk Ger Gynecol Assoc 2014; 15: 217-21)

Key words: PRES, intensive care unit, obstetrics patient

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Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinical entity characterized by temporary neurological symptoms, including acute headache, altered mental status, vision loss, and coma. Among the etiological factors associated with PRES are such diseases as hypertensive encephalopathy, preeclampsia/eclampsia/HELLP syndrome, immunosuppressive/cytotoxic drugs, acute or chronic renal disease, thrombotic thrombocytopenic purpura/hemolytic uremic syndrome, high-dose steroid therapy, liver failure/transplantation, endocrine dysfunction, hypercalcemia/hyperparathyroidism, bone marrow transplantation, massive blood transfusion/erythropoietin therapy, and porphyria (1, 2). Neuroimaging studies (MRI) in patients with PRES showed posterior cerebral edema (3-5). Following elimination of PRES-triggering factors and initiation of appropriate treatment, clinical and radiological findings usually resolve (6-8).

Most PRES cases occur concomitantly with acute or subacute neurological signs associated with convulsions. Usually, convulsions are initially local and then become generalized. Sometimes, seizures cause status epilepticus. In addition, changes in behavior and consciousness - ranging from somnolence and lethargy to stupor and coma - can occur. Moreover, various visual impairments, including hemianopsia, blurred vision, and cortical blindness, can be observed (1-4).

Patients with PRES are treated via provision of hemodynamic stability and hydration (intravenous crystalloid-colloids), maintenance of adequate arterial oxygen pressure, and improvement of electrolyte disturbances and coagulopathy (9). In patients with pulmonary aspiration, pulmonary edema, and hypoxemia, endotracheal intubation and mechanical ventilation are performed to maintain adequate oxygenation, while in those with impaired cardiac function, a central venous catheter may be required (10, 11). Although PRES is reversible when diagnosed and treated in a timely fashion, it can lead to neurological complications, including permanent brain damage and chronic epilepsy, when diagnosed at later stages (1, 2).

Herein, we present 7 pregnant patients diagnosed with PRES, based on clinical and radiological findings, who were treated in our intensive care unit during a 2-year period. Patient
records were retrospectively reviewed, and the medical treatment outcomes were evaluated in light of the literature.

**Material and Methods**

The study protocol was approved by the ethics committee. The clinical records of 7 patients (aged 20-36 years) who were diagnosed with PRES and treated at the intensive care unit of Firat University Medical School Hospital between July 2011 and July 2013 were retrospectively reviewed. The clinical diagnosis in all patients was made as previously described. Preeclampsia was diagnosed and classified according to American College of Obstetricians and Gynecologists (ACOG) criteria. Severe preeclampsia was defined as blood pressure ≥160/110 mm Hg, with either a urine dipstick showing 3+ or 4+ in a random urine sample or proteinuria ≥5.0 g during 24 h. Other evidence of severe disease included elevated serum creatinine, eclampsia, pulmonary edema, oliguria (<500 mL 24 h), fetal growth restriction, oligohydramnios, and symptoms indicative of significant end-organ involvement (headache, visual disturbance, and epigastric or right upper quadrant pain) (12). HELLP syndrome was defined based on the presence of hemolysis (serum LDH >600 IU/L, bilirubin >1.2 mg/dl, and the presence of schistocytes in peripheral blood), elevated liver enzymes (serum ALT and/or AST >70 IU/L), and thrombocytopenia (platelet count <100,000 mm<sup>3</sup>) after 20 weeks of gestation (13).

Cranial MRI (Signa Excite 1.5 T system (GE Healthcare, Milwaukee, WI, USA) using an 8-channel neuro-vascular head coil was performed in all patients after the onset of symptoms. Neuroimaging of the brain was performed via spin-echo T2-weighted (TR/TE/number of excitations =2880/126/2), spin-echo T1-weighted (460/14/2), and T2-FLAIR-weighted MRI (TR/TE/number of excitations =8800/2000/126/2) in the axial, sagittal, and coronal planes with 5-mm slice thickness. In addition, cranial MRI and detailed neuropsychological test (EMG, EEG, NCV, VEP-BERA, and TCD) findings obtained 1 month post-treatment were evaluated in each patient.

**Results**

The clinical and radiological findings are summarized in the Table 1. The mean age of the patients was 26.85±7.10 years

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**Table 1. The clinical and radiologic findings and treatment in the PRES patients**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Age (years)</th>
<th>G/P/A (n)</th>
<th>Clinical diagnosis</th>
<th>Gestational age (weeks)</th>
<th>Neurological symptoms</th>
<th>Status epilepticus</th>
<th>Location of T1-Hypo/ T2-Hyper intense abnormalities</th>
<th>ICU therapy</th>
<th>Time to remission (d)</th>
<th>Time to MV (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21</td>
<td>1/0/0</td>
<td>Eclampsia</td>
<td>31</td>
<td>Convulsions, Confusion, Headache Amlodipia</td>
<td>No</td>
<td>Bilateral Occipital</td>
<td>Thiopental, Esmolol, Magnesium</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>1/0/0</td>
<td>Eclampsia</td>
<td>39</td>
<td>Convulsions, Headache</td>
<td>Yes</td>
<td>Bilateral Occipital</td>
<td>Thiopental, Esmolol, Magnesium, Amlodipine</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>33</td>
<td>4/3/0</td>
<td>HELLP Syndrome</td>
<td>26</td>
<td>Convulsions, Headache</td>
<td>No</td>
<td>Left Basal Ganglia, Cerebellum</td>
<td>Thiopental, Esmolol, Magnesium, Amlodipine</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>34</td>
<td>1/0/0</td>
<td>Eclampsia</td>
<td>36</td>
<td>Convulsions, Headache</td>
<td>Yes</td>
<td>Bilateral Occipital Cerebellum</td>
<td>Thiopental, Esmolol, Magnesium, Amlodipine</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>21</td>
<td>1/0/0</td>
<td>Eclampsia</td>
<td>31</td>
<td>Convulsions, Headache</td>
<td>No</td>
<td>Bilateral Parieto-Occipital and Bilateral Basal Ganglia</td>
<td>Thiopental, Esmolol, Magnesium, Amlodipine</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>23</td>
<td>2/1/0</td>
<td>Severe Preeclampsia</td>
<td>36</td>
<td>Headache</td>
<td>No</td>
<td>Bilateral Occipital</td>
<td>Esmolol, Magnesium, Amlodipine</td>
<td>2</td>
<td>Ø</td>
</tr>
<tr>
<td>7</td>
<td>36</td>
<td>3/0/2</td>
<td>Eclampsia</td>
<td>31</td>
<td>Headache, Convulsions, Blurred Vision</td>
<td>Yes</td>
<td>Bilateral Cerebellar, Frontal, Parietal, Frontal, Occipital</td>
<td>Thiopental, Esmolol, Magnesium, Amlodipine</td>
<td>15</td>
<td>10</td>
</tr>
</tbody>
</table>

PRES: posterior reversible encephalopathy syndrome; G: gravidity; P: parity; A: abortus; ICU: intensive care unit; MV: mechanical ventilation

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(range: 20-36 years). The etiology of PRES was as follows: eclampsia: n=5 (72%); severe preeclampsia: n=1 (14%); and HELLP syndrome: n=1 (14%). Among the patients, hypertension (160-210/110-130 mm Hg), headache, and altered consciousness (ranging from confusion to coma) were observed. In all, 1 patient had blurred vision (14%) and 3 had status epilepticus (43%). Cranial MRI showed edema localized mainly to the posterior cerebral region. In addition, the cerebellum; basal ganglia; and frontal, parietal, and occipital lobes were affected to varying degrees (Figure 1).

Calcium channel blockers (amlodipine [Norvasc; Pfizer, Istanbul, Turkey] 10 mg/d, enteral) and β-blockers (esmolol [Brevibloc, Eczacibaşı-Baxter, Istanbul, Turkey] 50-200 mg/kg/min, parenteral) were administered to treat hypertension. Parenteral magnesium sulfate (Osel Drug, Istanbul, Turkey) (4-6 g 20/min IV and 1-2 g/h infusion) was administered to all patients. Moreover, all patients but 1 (case 6) were treated with thiopental sodium (I.E. Ulagay, Istanbul, Turkey) (2-4 mg/kg bolus, followed by infusion of 3-5 mg/kg/h for 24-48 h) to control sedation and convulsions (Table 1). In total, 5 patients received mechanical ventilation support for 1-3 d, 1 patient required mechanical ventilation for 10 d (SIMV, f:12/min; FiO2: 40, TV: 7 mL/kg, PEEP: 5 cm H2O, I/E: 1/2), and 1 patient did not require mechanical ventilator support.

All patients but 1 improved neurologically 2-5 d after PRES was diagnosed. The patient who required mechanical ventilator support for 10 d regained consciousness on d 10; however, she had speech impairment that lasted 15 d and improved at the end of the first month. After discontinuing mechanical ventilation, all patients were given parenteral magnesium sulfate. The magnesium level in each patient was monitored and maintained in the therapeutic range (4.8-8.4 mEq/L), and deep tendon reflexes, respiratory rate, and urine output were observed hourly. Patients whose general condition improved were transferred to the obstetrics and gynecology clinic to continue their treatment. Cranial MRI findings 1 month later were normal (Figure 2). None of the patients had intracranial pathologies, such as fatal subarachnoid hemorrhage due to negative results. Long-term evaluation (>1 year) was possible in 3 of the patients, and neuropsychological dysfunction was not observed.

Discussion

In the present study, the records of 7 pregnant women who were diagnosed with PRES, based on clinical and neuroimaging findings, and treated in the anesthesia intensive care unit of Firat University Medical School Hospital between July 2011 and July 2013 were retrospectively reviewed. PRES was first described by Hinchey (1) as a sudden increase in blood pressure due to a defect in the autoregulation of posterior circulation that causes clinical symptoms, including headache, generalized seizures, visual disturbances, lethargy, confusion, stupor, changes in mental status, and focal neurological signs. The diagnosis of PRES is made based on clinical and radiological findings (1).

All patients in the present study were diagnosed with PRES based on clinical and radiological findings and had pregnancy-related preeclampsia and/or HELLP syndrome. In addition, all but 1 of the patients had generalized seizures, and 3 patients had status epilepticus. Moreover, 1 patient had blurred vision and speech impairment that lasted 15 d. One patient that was diagnosed with PRES based on radiological findings (hyperintensity in T2-weighted sequences of the bilateral occipital region) had only headache as a neurological symptom, whereas the other patients had widespread neurological symptoms. Cranial CT can be used to diagnose hypodense lesions of posterior encephalopathy; however, MRI is the gold standard for diagnosing PRES (1-3). Currently, PRES is diagnosed...
more frequently than in the past due to the ubiquity of MRI. During the acute phase of PRES, hyperintensity is observed in T2-weighted MRI sequences, and iso-hypointensity is observed in T1-weighted sequences of gray and white matter. PRES primarily affects the parietal-occipital lobe; however, the cerebellar hemispheres, basal ganglion, frontal lobes, and brainstem are also frequently affected (1, 2, 14). Diffusion-weighted MRI is more sensitive to changes in the distribution of brain fluid, can detect edema in white matter during early-stage PRES, and is more reliable for differentiating between vasogenic edema and cytotoxic edema in PRES patients (3, 14). In patients with clinical symptoms suggestive of PRES, T2-weighted MRI sequences showed hyperintensity anomalies, especially in the occipital, parietal, and frontal lobes; cerebellum; and basal ganglia. The pathogenesis of PRES is not fully understood, but it is likely to be associated with endothelial damage and disruption of cerebral autoregulation. Accordingly, edema that is reversible has been suggested to occur in PRES due to impaired autoregulation associated with hyperperfusion and blood-brain barrier disruption without infarction (15-18). When increased systemic blood pressure exceeds cerebral autoregulatory mechanisms, it increases the permeability of the blood-brain barrier, thereby causing extravasation of fluid and blood into the brain parenchyma (6, 19). Elevated blood pressure leads to focal dilation in cerebral blood vessels, exceeding the upper limit of autoregulation; consequently, both vasodilation and vasoconstriction develop in these regions (20, 21). Another theory of the development of PRES is that cerebral artery spasms, ischemia, and cytotoxic edema are caused by acute hypertension due to a decrease in cerebral blood flow (9). With the appropriate treatment, most PRES patients completely recover within a few weeks (1). Delays in the diagnosis and treatment can negatively affect brain tissue, resulting in permanent neurological damage (5, 22-25). Sometimes, even with appropriate treatment, full recovery may not be achieved (26-28). In particular, ischemia can complicate the clinical picture, whether or not posterior encephalopathy with vasospasm and infarction are present (29). Full clinical remission was achieved in 2-5 d in 6 of the 7 presented patients, and MRI scans obtained 1 month later indicated that radiological remission was achieved in all patients. The intensive care process was delayed in 1 patient in the present study; she received mechanical ventilation support for 10 d, remission was delayed for up to 15 d, and her speech impairment persisted, even after she regained consciousness. This patient had the most common radiological involvement. If elevated systemic blood pressure is left untreated, it can cause the development of or aggravation of cerebral edema. In such patients, mean arterial blood pressure should be maintained at 105-125 mm Hg. Nicardipine and labetalol are usually the first-choice drugs for the treatment of hypertension. Fenoldopam mesylate is a selective dopamine-1 agonist that can also prevent renal failure. Nitroglycerin is also frequently used in such patients but was reported to aggravate brain edema by causing vasodilation in the brain (30). Sodium nitroprusside, hydralazine, diazoxide, and nimodipine, which is reported to have neuroprotective effects, may also be useful for lowering blood pressure (31, 32).

Esmolol (a β-1 selective adrenoceptor antagonist) was recently reported to potentially inhibit an increase in catecholamines and to have neuroprotective effects by causing changes in the immune system (33). In the present study, parenteral esmolol was administered in addition to an enteral calcium channel blocker (amlodipine) to all 7 PRES patients in order to maintain their mean arterial pressure at 110 mm Hg. Magnesium sulfate, propofol, benzodiazepines, phenytoin, barbiturates, and fosphenytoin can be used to treat refractory status epilepticus in pregnant women. In addition to general systemic supportive care, magnesium sulfate is considered to be the mainstay of refractory status epilepticus treatment in pregnant women. Magnesium sulfate increases vasodilation, thus decreasing calcium-dependent vasoconstriction and increasing cerebral blood flow, which prevents ischemic attacks that cause coma (34, 35). Patients with refractory status epilepticus are usually treated with continuous infusion of midazolam, propofol, or barbiturates (36). In the present study, patients with generalized convulsions or status epilepticus were treated in the intensive care unit via endotracheal intubation, followed by thiopental infusion (2-4-mg/kg bolus followed by 3-5 mg/kg/h infusion for a period of 24-48 h) and mechanical ventilation support. The duration of mechanical ventilator support in the present study’s patients was determined according to the severity of the clinical and radiological findings. In addition, after discontinuation of mechanical ventilation, patients were given a magnesium sulfate infusion (monitored to be in the therapeutic range of 4.8-8.4 mEq/L) for 1 d.

In conclusion, PRES is a clinical condition with a multifactorial etiology, is characterized by varying clinical symptoms, and is diagnosed via radiological imaging techniques. PRES can be diagnosed clinically and radiologically in cases of a sudden increase in blood pressure and consequent neurological conditions, such as headache, generalized seizures, visual disturbances, lethargy, confusion, stupor, and changes in mental status caused by the disruption of autoregulation of posterior circulation. We think that timely supplementation of thiopental infusion to antihypertensive and magnesium sulfate treatment can improve the clinical status faster and more efficiently in patients diagnosed with PRES who experience generalized seizures.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of noninvasive studies.

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.


Conflict of Interest: No conflict of interest was declared by the authors.

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