FACTA UNIVERSITATIS
Series: **Medicine and Biology** Vol. 16, No 2, 2014, pp. 96–99 UC 618.2:616.12-008.331.1

PRES AS A COMPLICATION OF A MODERATE PREECLAMPSIA: CASE REPORT AND SHORT REVIEW OF LITERATURE

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Abstract. *We present a case of puerpera with two major complications of preeclampsia: PRES manifested by eclampsia and HELLP syndrome. PRES is neuroradiological entity characterized by hypertension, altered mental status, visual disturbances, headache and generalized seizures together with characteristic findings on cerebral magnetic resonance imaging scan. An important fact considering PRES (which also happened to our patient) is that it can be developed without significant rise in blood pressure, in a situation of severe endothelial injury with diminished cerebral autoregulatory capacity. Another consequence of vascular endotheliosis that developed in our patient was HELLP syndrome. Although the complications are severe, this state is usually completely reversible presuming that prompt diagnosis and adequate therapy were timely undertaken, as in the case we report here.*

Key words: *Eclampsia, posterior reversible encephalopathy syndrome, HELLP syndrome*

Introduction

Preeclampsia is a disorder that complicates 5–8% of all pregnancies [1–7]. Together with its most serious complications: pulmonary edema, acute renal failure, disseminated intravascular coagulation (DIC), syndrome of haemolysis, elevated liver enzymes and low platelets (HELLP), eclampsia, it is one of the leading causes of maternal and fetal morbidity and mortality (10–15% of all maternal deaths) [2, 7].

Genetic predisposition, immunologic intolerance between maternal and fetoplacental tissues and insufficient placentation lead to placental ischemia. This provokes abnormal nitric oxide and lipid metabolism, leukocyte and coagulation system activation, changes in various cytokines etc., resulting in generalized vasospasm and vascular endotheliosis [1, 2, 5, 6, 8–10]. Dominating symptom is hypertension, accompanied by significant proteinuria.

In this article we present a case of puerpera with two major complications of preeclampsia – posterior reversible encephalopathy syndrome (PRES), manifested by eclampsia, and HELLP syndrome.

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Case Report

A 23 years old primipara was admitted to our intensive care unit (ICU) 21 hours after spontaneous term delivery, when she gave birth to a live male child (3500 g / 53 cm, Apgar score 9) in her hometown hospital. First sixteen hours after delivery passed uneventfully; suddenly she lost conscience and suffered generalized tonic―clonic seizure. After a few minutes she regained consciousness, but remained disoriented. Blood pressure (BP) measured at that moment was 160/100 mm Hg. Ninety minutes later she suffered another seizure, after which she was transferred to our hospital.

On admission she was in the state of somnolence (during the transport she was given midasolam 45 mg), but oriented, able to adequately respond to our questions and obey commands. She claimed to be healthy till the day of the delivery, with no illness of any kind. She regularly visited her gynecologist during the pregnancy.

Physical examination on admission showed no pathological signs or symptoms, other than somnolence and hypertension – BP was 160/100 mm Hg, pulse rate 73 bpm. Venous blood samples were taken for hematological and biochemical analyses, and were repeated every day during her stay at our hospital.

On admission the results of the laboratory analyses out of the reference ranges were as follows: Hb 86 g/l, Ht 27%, Plt 70 × 10^9/l, indirect bilirubin 15.2 μmol/l, total proteins 49.5 g/l, albumins 22.3 g/l, ALT 74 U/l, AST 138 U/l, LDH 1339 U/l, serum Fe 83 μmol/l, CRP 46,9 mg/l.

24 hours later the results out of reference range were as follows: Hb 83 g/l, Ht 26.9%, Plt 103 x 10^9/l, total proteins 51 g/l, albumins 26 g/l, AST 71 U/l, LDH 716 U/l, serum Fe 21 μmol/l, haptoglobin 0.47 g/l; reticulocytes 10%, schistocytes on peripheral blood smear were found. The next day all results were in referent range, except Hb 75 g/l and Ht 24%.

Endocranial MSCT was done immediately after the admission: irregular, partly confluent hypodensity zones, in cortical and subcortical white matter that might correspond to PRES changes were detected in parieto-occipital regions bilaterally. Pons, cerebellum and mesencephalon showed no morphological changes. No presence of blood endocranially.

In order to get more subtle evaluation, magnetic resonance imaging (MRI) was done the next day (T1W sagittal, T2W/T2W FLAIR/ DW1 transversal and T2W coronal endocranial tomograms): zones with increased signal intensity, that correspond to PRES, were found in bilateral frontal, parietal and occipital regions in subcortical white matter (Figs. 1 and 2). There were no other pathological changes.

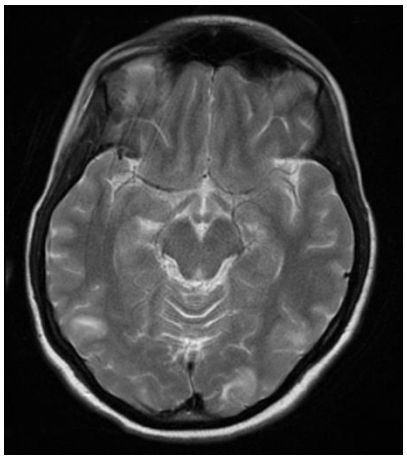

Fig. 1. Multiple cortico-subcortical areas of T2-weighted hyperintense signal involving the occipital lobes bilaterally in axial plane

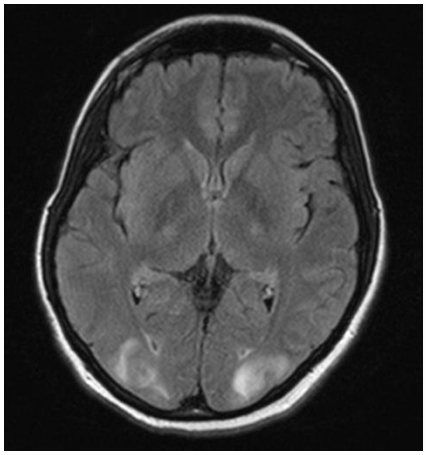

Fig. 2. Multiple cortico-subcortical areas of FLAIR-weighted hyperintense signal involving the occipital lobes bilaterally in axial plane

The patient was continuously monitored: BP, pulse rate, oxygen saturation, temperature, diuresis. All parameters were in normal range, except moderate to severe hypertension.

Antiedematous (sol. Manitholi 20% 125 ml/6h, dexamethasone 4 mg/8h), anticonvulsive (sol. $MgSO_4$ 1g/hour), antihypertensive, antibiotic, uterotonic and anticoagulant - low molecular weight heparin (LMWH) therapy was immediately started, as well as albumin, electrolyte and erythrocyte supplementation (according to laboratory results):

On the first day, there was one BP elevation to 170/110 mmHg, which was treated with urapidil 50 mg iv. The dose was sufficient to reduce BP to 130/80 mmHg, so we further proceeded with peroral therapy: Captopril 25 mg/12 hour which successfully kept BP between 120/80 and 140/90 mmHg.

During her stay at our Clinic, the patient had no eclamptic seizures, her laboratory results improved as well as her clinical state, so after five days she was transferred back to her hometown hospital.

Discussion

The presented case seems to be a good illustration of the complications that could be expected of the state we considered to be only the moderate form of preeclampsia. Preeclampsia can be manifested by wide range and intensity of symptoms – from severe hypertension and proteinuria, to mild or absent hypertension without proteinuria. According to recent data, 20% of women who developed eclampsia did not have any premonitory symptoms before the onset of convulsions; 16% of patients did not have diastolic blood pressure higher than 90 mmHg [11, 12].

Our patient (per anamnesis) did not have any obvious typical signs of preeclampsia till after the labour. Sixteen hours after the delivery her state deteriorated suddenly (with no prodromal signs) and she had two episodes of eclamptic seizures. Elevated blood pressure was registered for the first time. PRES was diagnosed on MRI scan.

PRES is a relatively new neuroradiological entity (first described by Hinchey at al. 1996.), characterized by clinical signs and symptoms of hypertension, altered mental status, visual disturbances, headache and generalized seizures together with characteristic findings on MRI scan [3, 13–20]. Besides eclampsia, PRES can occur in sepsis, after exposure to immunosuppressants, in autoimmune/renal/hypertensive diseases [13, 14, 21–24]. Underlying disorders in these conditions are immune system activation, inflammatory response, vascular instability and endothelial cell disfunction [13, 14, 17, 19, 22–24].

It is supposed that rapid rise in blood pressure, in a state of already compromised blood brain barrier (endothelial dysfunction) leads to breakthrough of cerebral blood flow autoregulation, forced dilatation of cerebral vessels, cerebral hyperperfusion and vasogenic cerebral edema [3, 14, 21, 23, 24]. Some findings,

though, suggest that neurological symptoms arise from "overautoregulation", vasospasm, hypoperfusion, that causes ischemia and, again, cerebral edema [14, 15, 21, 23–25]. Posterior brain is less innervated with sympathetic fibers that regulate cerebral blood flow, so parieto-occipital white matter is the region where the edema most frequently occurs, but changes can be also found in frontal lobes, basal ganglia, cerebellum, and brainstem [14, 17, 23]. T2 weighted MRI demonstrates regions of higher intensity, suggestive of vasogenic edema [13–17, 19–21,].

Very important fact considering PRES is that it can develop without a significant rise in BP [3, 14, 17, 22]. This is especially true in pregnancy, where the cerebral autoregulation curve is shifted to the lower range of BP [3, 14, 20, 26]. In cases of severe endothelial injury, as in preeclampsia, autoregulatory capability is completely diminished, so, as in our case, even a moderate elevation in BP (160/100 mmHg) can cause neurologic symptoms, culminating in eclamptic seizures. For that reason, in 2011, American College of Obstetricians and Gynecologists (ACOG) Committee [27] stated that: "Acute onset of severe systolic (more than 160 mmHg) or severe diastolic (110 mmHg) hypertension, or both, in pregnant women, persistent more than 15 minutes, is considered hypertensive emergency". The most important predictor of cerebral injury is systolic tension [3, 5, 25].

What is encouraging about PRES is that this state is usually completely reversible within 7 days, presuming that prompt control of seizures and BP and expeditious delivery (in cases of prepartal eclampsia) were undertaken [3, 13, 14, 18, 21, 25]. Our therapy regimen included antiedematous therapy (sol. Manithol 20% 125 ml/6h, Dexamethasone 4 mg/8h) and anticonvulsive therapy (Magnesium sulfate infusion 1 g/h). Magnesium is considered the drug of choice for seizure prophylaxis and control in eclapmsia [1–3, 7, 17, 23, 26–28]. Because of toxic effects of hypermagnesemia (cardiac arrhythmia and respiratory depression), magnesemia, diuresis and deep tendon reflexes should be closely monitored.

Antihypertensive therapy in pregnancy and lactation is highly limited, because of drug effects on the fetus as well as on maternal circulation. Sudden reduction of BP can compromise fetal-placental circulation, so, even in cases of emergency, only 10% BP reduction is recommended during first hour and another 15% gradually over next 2–3h [29–33]. The first choice drug is intravenous labetolol, followed by hydralazine, nicardipine (in cases of cerebral vasospasm), sodium nitroprusside (only in most refractory cases), nitroglycerin (especially in pulmonary edema) and nifedipine per os [2, 4, 6, 7, 18, 26, 28–37]. Urapidil is allowed in pregnancy as well and it seemed to be a good choice in case of our patient, when raised intracranial pressure was presumed and cerebral vasodilatation was to be avoided [35, 36]. The urapidil dose of 50 mg was effective enough and allowed us to switch to peroral therapy with captopril 25 mg/12h. ACE inhibitors are contraindicated in pregnancy, but enalapril and captopril are allowed during lactation [5, 6, 10, 32, 34–36]. Considering the fact that renin–angiotensin–aldosteron system is also affected in preeclampsia, we chose captopril and had a satisfactory effect.

The same patient suffered from another consequence of damaged vascular endothelium: syndrome of hemolysis (LDH level over 600 IU/l), elevated liver enzymes (AST and ALT levels higher than 70 IU/l) and low platelet count (below 150×10^9 /l) – HELLP syndrome [2, 7, 38, 39]. HELLP is a complication in 10–15% cases of eclampsia and up to 20% of cases of early onset antepartum eclampsia [12, 40, 41]. It represents a serious complication of pregnancy that might cause maternal acute renal failure, peripartal hemorrhage, and fetal intrauterine growth restriction (IUGR), fetal thrombocytopenia, hemorrhage and death. HELLP demands prompt fetal delivery and removal of the placenta (as placenta is the primary cause of toxemia). Our patient had all diagnostic parameters of HELLP on admission. Hemolysis was proven by elevated LDH levels. Low haptoglobin level is even better marker of hemolysis; in our case the level was near lower limit. It would have been interesting to know her previous results, but unfortunately they were not available. Symptoms of the disease resolved rather quickly. We presume that it was (besides the fact that pregnancy was terminated and placenta, the main cause of the disease, removed) partly because of prompt treatment and may be because it was the case of late onset preeclampsia, which has a more favorable clinical course compared to the early onset preeclampsia.

Conclusion

We emphasized that it is important to keep in mind that eclampsia can develop even with moderate elevation of BP. If PRES is not adequately diagnosed and treated, ischemic cerebral injury and irreversible neurological damage could develop, as well as impaired cognitive function later in life. With prompt seizure and BP control, the process is completely reversible.

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