Acute cortical blindness in preeclampsia – a case of reversible posterior encephalopathy syndrome

Ostra ślepota korowa w stanie przedrzucawkowym – przypadek zespołu odwracalnej tylnej encefalopatii

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Abstract

Background: *Cortical blindness is one the most disturbing symptoms of reversible posterior encephalopathy syndrome in preeclamptic and eclamptic patients. The disease has been previously associated with a hypertensive breakthrough in the autoregulation of posterior cerebral arterioles followed by extravasation of the fluid into the brain tissue.*

Case: *22-year-old primigravida in the 39th week of gestation diagnosed with gestational diabetes mellitus presented with mild preeclampsia and was admitted to our hospital. Antihypertensive treatment was initiated. Her blood pressure remained between 120/80 to 140/90 mm Hg. Glucose levels were within acceptable range. Before the labor induction she developed acute cortical blindness. Magnetic resonance imaging showed vasogenic edema localized in occipital lobes. Cesarean section was performed and anti-edematous treatment initiated. Blindness resolved by the fifth day postpartum.*

Conclusions: *Reversible posterior encephalopathy developed in our patient in spite of normalized blood pressure that remained within autoregulation limits. Alternative pathogenesis and precipitating factors are discussed.*

Key words: **pre-eclampsia** / **cortical blindness** / **vasogenic brain edema** / / **magnetic resonance imaging** / **gestational diabetes mellitus** /

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Streszczenie

Wstęp: *Ślepota korowa jest jednym z najbardziej niepokojących objawów zespołu odwracalnej tylnej encefalopatii u pacjentek w stanie przedrzucawkowym lub z rzucawką. Zespół ten był pierwotnie wiązany z przełamaniem autoregulacji tylnych tętniczek mózgowych przez bardzo wysokie wartości ciśnienia tętniczego. Następujące wynaczynienie płynu do tkanki mózgowej miało powodować ubytkowe objawy neurologiczne.*

Przypadek: *22-letnia pierwiastka ze zdiagnozowaną cukrzycą ciążową zgłosiła się w 39 tygodniu ciąży do Oddziału Patologii Ciąży z łagodnym stanem przedrzucawkowym. Włączono leczenie przeciwnadciśnieniowe. Wartości ciśnienia tętniczego utrzymywały się w granicach 120/80 do 140/90 mmHg. Wyrównanie glikemii było zadowalające. Przed indukcją porodu u pacjentki doszło do nagłego zaniewidzenia. Zdiagnozowano ślepotę korową i wykonano rezonans magnetyczny głowy uwidaczniając obrzęk naczyniopochodny zlokalizowany w płatach potylicznych. Pacjentkę rozwiązano drogą cesarskiego cięcia i włączono leczenie przeciwobrzękowe. Objawy ustąpiły całkowicie w piątej dobie pooperacyjnej.*

Wnioski: *Zespół odwracalnej tylnej encefalopatii rozwinął się u naszej pacjentki mimo znormalizowanych wartości ciśnienia tętniczego pozostających w granicach mózgowej autoregulacji. Poddano dyskusji alternatywne mechanizmy patogenetyczne i czynniki predysponujące.*

Słowa kluczowe: **stan przedrzucawkowy** / **ślepota korowa** /
/ **naczyniopochodny obrzęk mózgu** / **magnetyczny rezonans jądrowy** /
/ **cukrzyca ciążowa** /

Introduction

Visual impairment in severe preeclampsia is estimated to occur in nearly 15% of patients and may be caused by posterior reversible encephalopathy syndrome (PRES) [1]. This neurotoxic state was first described by Hinchey et al. as a condition affecting acutely ill patients with hypertension, preeclampsia or eclampsia, renal insufficiency and undergoing immunosuppressive therapy [2]. Symptoms of this disorder include headache, altered mental functioning, seizures and loss of vision. Magnetic resonance imaging (MRI) in PRES shows cortical and subcortical hyperintense areas consistent with edema in T2-weighted and fluid attenuated inversion recovery (FLAIR) images localized primarily in posterior regions of cerebral hemispheres. MRI is regarded as the imaging modality of choice for diagnosis of this syndrome [3].

The most widely acknowledged theory on pathogenesis of PRES involves a hypertensive breakthrough in the autoregulation of posterior cerebral arterioles followed by extravasation of the fluid into the brain tissue. Posterior cerebral vessels seem more susceptible to hypertensive changes because of their less abundant sympathetic innervation [4].

We describe a clinical course in a pregnant patient with gestational diabetes mellitus (GDM) and mild preclampsia who developed cortical blindness related to PRES.

Case

22-year-old Caucasian woman was admitted for mild preeclampsia to a high risk pregnancy ward of our hospital in the 39th week of her first pregnancy.

Her pregnancy was complicated by GDM (gestational diabetes mellitus). She was diagnosed in the 30th week of gestation on a basis of abnormal oral glucose tolerance test (with 75g of glucose) with 2hr postprandial glycemia 231mg/dL. Initially low caloric diet was proposed as the sole treatment. Glucose levels were not monitored regularly. Even though, on interval checkup in the 34th week of gestation glycated hemoglobin concentration was 5.2%. The patient's pre-pregnancy body mass index was 23kg/m^2 and her weight gain in pregnancy was 14kg. Glucosuria was absent throughout pregnancy. Regular ultrasound examinations confirmed fetal growth within normal range. She never had proteinuria or elevated blood pressure until the last prenatal checkup when she presented with blood pressure 160/110 mm Hg and rapidly developing lower extremities edema. She had been prescribed oral methyldopa (250 milligrams three times a day) and referred to our department on the following day for further evaluation.

On admission, mildly elevated blood pressure (140/100mm Hg) and moderate lower extremities edema were diagnosed. The patient did not report visual disturbances, headache, nausea, abdominal pain or any other symptoms. Her medical history, apart from GDM, was unremarkable. She denied alcohol, tobacco, or illicit drugs use. General physical examination did not reveal any abnormalities. Obstetrical examination demonstrated a formed cervix with closed cervical canal and a single fetus in cephalic presentation. Amniotic sac was preserved. Uterus was soft and non-tender. The patient did not report any contractions. Non-stress test performed in admission room confirmed fetal-well being.

Laboratory panel was obtained. Complete blood count and serum aminotransferase activity were within normal range. Platelets count was 248K/uL (normal range: 140-440K/uL). Electrolytes examination showed mild hyponatremia – 131,9 mEq/L (normal range: 136-145mEq/L). Creatinine concentration was slightly elevated - 1.19mg/dL (normal range: 0,5-0,9mg/dL). Creatinine clearance calculated from the Cockroft-Goult formula was 75mL/min. Urea concentration was 28mg/dL (normal range: 0-50 mg/dL). Plasma protein concentration was low – 4,77g/dL (normal range: 6.4-8.3g/dL). Urinalysis showed marked proteinuria – 285mg/dL (normal range: max. 30mg/dL). Fasting glucose concentration was 116 mg/dL (normal range: 60-90 mg/dL). Activated partial thromboplastin time (APTT) was 29 seconds (normal range: 26-37 seconds), INR was 1,1 (normal range: 0.8-1.2) and fibrinogen concentration was 2.1g/L (normal range 1.8-3.5g/L).

Ultrasound examination revealed a single fetus in cephalic presentation. Estimated weight was 3100 grams. No fetal or placental abnormalities were found. Doppler assessment of middle cerebral artery and umbilical vessels showed normal flow patterns.

Due to unfavorable cervix and lack of indications for immediate delivery anti-hypertensive treatment was initiated with methyldopa titrated to achieve optimal effects (500 milligrams three times a day). Blood pressure measured every 4 hours remained within normal range (between 120/80 to 140/90 mm Hg). Fluid intake and diuresis were balanced. 24-hour proteinuria was 0,6 grams/24 hours. Patient's 1hr postprandial glycemia with strict diabetic diet was between 130-140mg/dL. In two measurements glycemia exceeded 140mg/dL (152 and 160mg/dL respectively) but dietary treatment was maintained after diabetological consultation. The patient reported no spontaneous contractions during treatment period. On repeat obstetrical examination cervical ripening was observed and the patient was qualified for labor induction with oxytocin infusion upon completion of 40th week of gestation.

On the day of induction before transfer to labor room and before the start of oxytocin infusion the patient started to complain of severe headache, she was agitated and strangely confused. After calming her down she admitted that she had suddenly lost her sight. Her blood pressure was 120/80mm Hg and all other vitals were normal. Emergency ophthalmological and neurological consultations were requested.

Patient's pupils were equal, round and bilaterally reactive without a relative afferent pupillary defect. She was found completely blind with no light perception. Extraocular movements were full, intraocular pressures and anterior segment examination were normal. Funduscopic examination of both eyes showed normal vascular pattern with bilateral faint retinal petechiae. Neurological examination did not reveal any additional abnormalities. Provisional diagnosis of acute cortical blindness was made and brain MRI was performed immediately.

MRI images in T2-weighted and FLAIR sequences demonstrated small hyperintense areas in both occipital lobes in cortical and subcortical localization - **Figure 1**.

Effacement of cerebral sulci in close proximity was observed. The overall MRI image was suggestive of vasogenic edema consistent with posterior reversible encephalopathy syndrome. During the diagnostic process blood pressure remained within normal range, electronic fetal heart monitoring was reassuring and no symptoms of eclampsia developed.

We performed cesarean section. Time between onset of blindness and operation was 4 hours. Just before the operation patient's blood pressure peaked to 185/115 and she was placed on continuous hydralazine infusion (up to a total dose 10 mg) throughout the procedure. Apparently healthy male infant weighing 3000 grams with Apgar scores of 9/9/9/9 was delivered. The operation was performed in general anesthesia. Blood pressure during the procedure balanced between 160/90 and 110/60mm Hg but stabilized afterwards. Blood loss was within usual range. Postoperative period was complicated by uterine relaxation and prolonged bleeding. Oxytocin was administered in continuous infusion up to a total dose of 20 units until the bleeding subsided. Two units of packed red blood cells and two units of plasma were transfused. There were no further obstetrical complications.

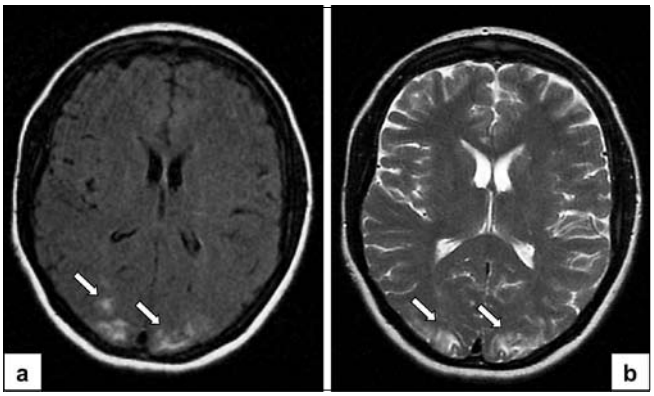

Figure 1. Magnetic resonance images in FLAIR (a) and T2-weighted (b) sequences. Hyperintense lesions consistent with vasogenic edema (arrows).

Anit-edematous treatment was initiated. It consisted of 20% mannitol solution (50mL four times a day), furosemide (40mg four times a day) and dexamethasone (8mg daily) given intravenously. Prophylactic postoperative dose of nadroparin was doubled to 15000 units daily to prevent cerebral blood flow impairment. Serial laboratory panels showed moderate increase in serum creatinine to 2.08mg/dL and significantly decreased plasma protein – 3.57g/dL. Proteinuria worsened on fourth postoperative day to 1100mg/dL but gradually improved thereafter. Albumin infusions were started at the dose of 100mL of 20% solution daily until protein concentration reached 5.3g/dL and remained stable. Negative fluid balance was maintained for first two days postpartum. Antihypertensive drugs were not necessary. No significant abnormalities in patient's blood count and aminotransferase activity developed. Patient's visual acuity was light perception on the first postoperative day and returned to normal by the fifth. Repeat funduscopic examination of both eyes showed normal vascular pattern with complete regression of previously reported changes. Creatinine levels normalized. Minor proteinuria – 50mg/dL – persisted. The patient was recommended nephrological checkup and discharged on fourteenth day postoperatively.

Discussion

Blindness in preeclampsia and eclampsia is a very disturbing symptom for both patient and tending physician. Following diagnoses must be considered: stroke, PRES, Purtscher's retinopathy, optic nerve edema, severe retinal detachment or various retinal vessels emboli (i.e. fat, amniotic fluid or air) [5]. Patient's charts should be reviewed for episodes of transient hypotension potentially causing irreversible posterior watershed infarct. Critical time would be the onset of spinal anesthesia especially in emergency setting or intravenous antihypertensive drugs infusions. [6]

PRES was diagnosed in our patient on a basis of distinctive MRI image and after exclusion of ophtalmological causes. Unlike most obstetrical cases described in literature which were related to severe preeclampsia our patient had mild disease and modest elevation of blood pressure controlled effectively with oral therapy before the onset of blindness. We have concluded that either cerebral autoregulation have been significantly disrupted or completely alternative pathogenesis must be considered.

Rosengarten et al. in their study on transcranial Doppler have shown that GDM is associated with an abnormal cerebral blood flow regulation [7]. Additionally, Cipolla et al. have shown that a rise in glucose concentration dilates cerebral arteries by an increased release of nitric oxide from endothelium [8]. This mechanism may counter neurogenic and myogenic vessel tone and thereby weaken the blood-brain barrier. However, in our patient both glycated hemoglobin concentration in the third trimester and blood glucose profile in the hospital setting were within acceptable range and there were no episodes of significant hyperglycemia. Our patient was neither obese nor overweight before pregnancy and her weight gain was moderate. Nevertheless, late onset of the hypertensive disease and lack of fetal or placental involvement suggest maternal type preeclampsia related to GDM [9]. Underlying vascular abnormalities may have contributed to the development of PRES.

Literature search revealed a growing body of evidence that the initially supported theory of autoregulatory failure may not explain clinical findings of PRES. More than 20% of patients who developed the syndrome were normotensive or had mildly elevated blood pressure well within autoregulation limits. Alternative pathogenetic theory involves a severe vasoconstriction causing "borderzone" endothelial hypoxia and increased vascular permeability [10]. This theory was an early concept of eclamptic neurotoxicity but is being successfully reinstated [11]. The generalized vasospasm and systemic inflammatory response are inherent components of preeclamptic disease and progress in spite of blood pressure control [12]. Further investigation is necessary to confirm this new standpoint.

We declare that we have no conflict of interest.

Piśmiennictwo

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