Case Report

Posterior reversible encephalopathy syndrome around pregnancy: Three cases and review of the literature

Cécile Choux[1,*], Anne-Sophie Gobenceaux[1], Maxime Samson[2], Yannick Béjot[3], Paul Sagot[1]

[1]Department of Obstetrics and Gynecology, Dijon University Hospital, France
[2]Department of Internal Medicine and Clinical Immunology, Dijon University Hospital, France
[3]Department of Neurology, Dijon University Hospital, France

Abstract

Posterior reversible encephalopathy syndrome is a transient clinical neuroradiological entity. Clinical signs include headache, vision changes, altered mental status and generalized seizure. Although well-known by neurologists, posterior reversible encephalopathy syndrome is under-recognized and undertreated by obstetricians because symptoms overlap with preeclampsia. Yet, correct and prompt diagnosis determines the prognosis as sequelae can occur if treatment is delayed. We report three cases of posterior reversible encephalopathy syndrome. The first was diagnosed during the post-partum period in a context of HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelet count). The second occurred during late pregnancy with preeclampsia, and the third was diagnosed 12 days after delivery.
The cases and the short review of the literature highlight the particularly challenging diagnosis of posterior reversible encephalopathy syndrome around pregnancy and its specific treatment.

Key words:

Blindness, brain edema, posterior leukoencephalopathy syndrome, preeclampsia, seizures

Introduction

Posterior reversible encephalopathy syndrome (PRES) is a transient clinical and radiological entity characterized by headache, blurred vision, altered mental status and seizures [1]. Several autoimmune and vascular conditions, including preeclampsia, can trigger PRES [1]. Herein, we report three cases of PRES, two of which occurred during the post-partum period.

* **Correspondence:** Cécile CHOUX
E-mail: cecile.choux@gmail.com
Address : Service de Gynécologie-Obstétrique
CHU de DIJON, 14, rue Gaffarel, 21079 Dijon, France
Tel: +33 3 80 29 38 52
**Fax:** +33 3 80 29 36 64

Case presentation

Case 1

A 33-year-old woman, gravida 7 para 1, whose past history included Grave's disease, smoking and obesity, had preeclampsia during her first pregnancy and delivered a low-birth-weight girl. She then had five miscarriages despite negative screening for vascular diseases. The pregnancy presented here was uneventful until 29 weeks of gestation (WG). She was admitted because of preeclampsia complicated by intrauterine growth restriction (IUGR), oligohydramnios, umbilical cord and cerebral Doppler abnormalities and reduced fetal heart rate (FHR) variability. The woman had elevated blood pressure (BP) at 140/90 mmHg but no other clinical signs. Three-hour continuous FHR monitoring was considered normal and led to an expectant attitude. Biological findings (including haemoglobin, platelets and liver enzymes) were normal except for significant proteinuria

(1.4 g/L). Eight hours later, unexpected Intra-Uterine Fetal Death (IUFD) was diagnosed. Labor induction led to the vaginal delivery of a stillborn weighting 895 grams.
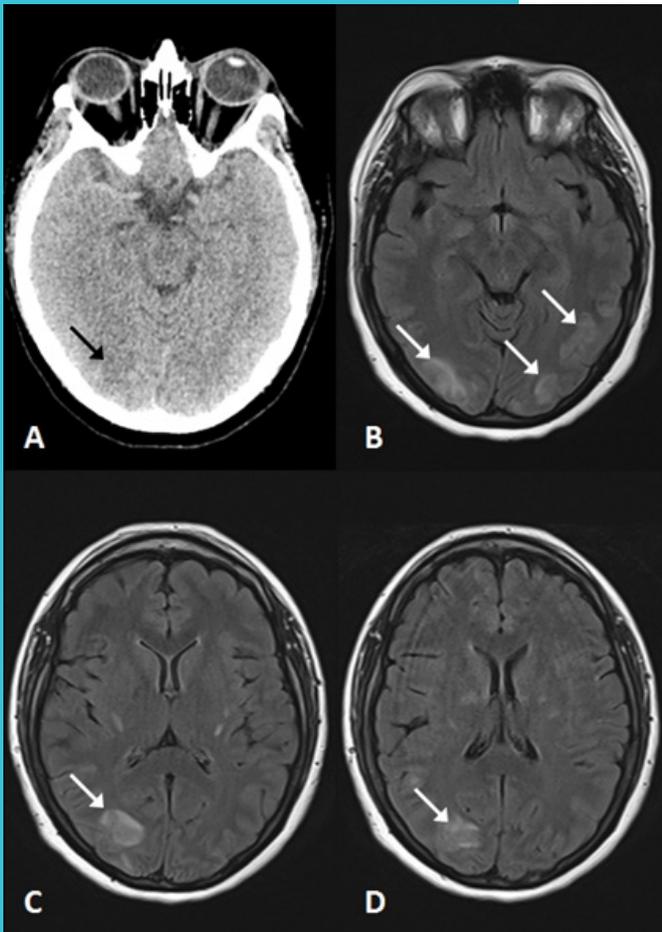
Cerebral CT-scan showing low density areas in the subcortical white matter of the right occipital lobe (black arrow) (A). Cerebral MRI (T2 FLAIR) showing high signal intensity abnormalities (white arrows) (B, C, D).

Twenty-four hours later, the woman reported an increasingly severe posterior headache, photophobia, tinnitus, and blurred vision rapidly leading to vision loss. BP remained elevated despite intravenous nicardipine. Examination revealed major anxiety, brisk deep tendon reflexes and total blindness despite normal pupil reflexes. Blood tests revealed thrombocytopenia, elevated liver enzymes and hemolysis, which led to a diagnosis of HELLP syndrome. Proteinuria had increased to 5.2 g/day. Intravenous magnesium sulfate therapy was started. Cerebral CT-scan and CT-angiography (CTA) ruled out intra-cranial hemorrhage, thrombophlebitis or cerebral vasoconstriction but showed low-density areas involving the subcortical white matter of the right occipital lobe (Figure 1A). PRES was thus suspected. The diagnosis was confirmed by T2-weighted and fluid-attenuated inversion recovery (FLAIR) images (Figure 1B-D), which showed multifocal and bilateral high signal intensity abnormalities in the white matter that were more prominent in the right and posterior areas. Diffusion-Weighted Imaging (DWI) sequences showed an unreduced Apparent Diffusion Coefficient (ADC), which suggested vasogenic edema. Nimodipine (1 mg/h) was started. Three hours later, the biological parameters worsened: thrombocytopenia was 50.109/L, alanine amino transferases 300 IU/L, aspartate amino transferases 433 IU/L and haptoglobin < 0.08 g/L. Under treatment, the visual disturbances had resolved completely within 48 hours and blood samples were normal after five days. Nimodipine was pursued orally. Three months later, the clinical examination and cerebral MRI were normal.

Case 2

A 16-year-old primigravida with an uneventful pregnancy was admitted at 40 WG because of faintness and confusion. BP was 152/98 mmHg. Haptoglobin, platelets and hepatic tests were normal. Serum albumin was 21 g/L, uric acid 609 μmol/L and proteinuria 5 g/L. Within two hours, she presented two generalized seizures. As she had already suffered from seizures, she was diagnosed as epileptic and levetiracetam was started. Labor was induced with ocytocin. Blood pressure remained elevated (160/100 mmHg) and deep tendon reflexes were brisk. Intravenous magnesium sulfate was thus started. She delivered a eutrophic healthy girl. Cerebral CT-scan found bilateral asymmetric parieto-occipital edema suggesting PRES (Figure 2A) whereas the CTA ruled out cerebral vasoconstriction. Intravenous nimodipine was therefore implemented. Magnetic resonance imaging (MRI) confirmed the diagnosis (Figure 2B-D). The following day, the BP and neurological exam were

normal and proteinuria was 0.2 g/day. Magnesium sulfate was stopped. Nimodipine and levetiracetam were continued orally. Questioning after the delivery revealed that she had suffered from intermittent blurred vision and frontal headaches for four days before the admission.

Figure 2.
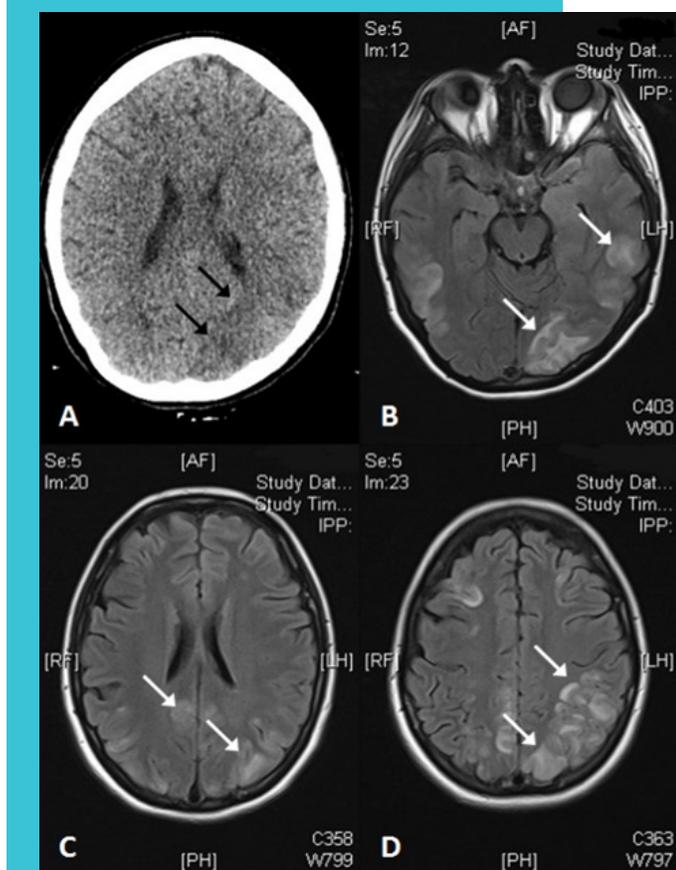
Cerebral CT-scan showing bilateral asymmetric parieto-occipital edema, which is more prominent in the left occipital area (black arrows) (A). Cerebral MRI (T2 Flair) showing high signal intensity abnormalities (white arrows), more prominent on the left side (B, C, D).

Case 3

A 21-year-old patient, gravida 2 para 1 with no remarkable past history, suffered from right-sided headaches eight days after giving birth to a eutrophic healthy boy. Four days later, the headaches increased and three episodes of confusion and generalized seizure occurred. BP on admission was 140/100 mmHg. No clinical or biological evidence of preeclampsia or HELLP syndrome was found. The CT scan and CTA were normal. FLAIR images showed frontal and occipital bilateral high signal intensity abnormalities in the white matter (Figure 3). DWI sequences found high intensity signals with increased ADC. These observations suggested vasogenic edema, thus confirming the diagnosis of PRES. Levetiracetam, nimodipine, clonazepam and magnesium sulfate were started. The evolution was favorable and she was discharged 12 days later, free of treatment except for levetiracetam, which was maintained.

Figure 3.
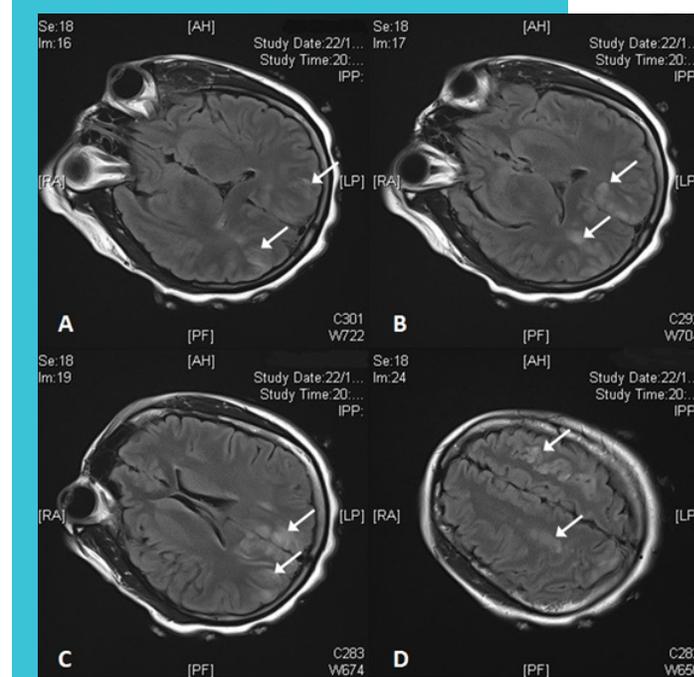
Cerebral MRI (T2 FLAIR) showing bilateral high signal intensity abnormalities in the frontal and occipital areas (white arrows).

Discussion

Although PRES has gained substantial recognition since its initial description by Hinchey et al. as a "Reversible posterior leukoencephalopathy syndrome" [1], this rare condition is still under-recognized and

undertreated, and its exact frequency is unknown. The underlying pathophysiology of PRES has not yet been clarified. Two hypotheses are proposed to explain brain edema [2]. In the vasogenic theory, hypertension with overwhelmed autoregulation could trigger acute disruption of the blood-brain barrier, thus leading to focal vasogenic cerebral edema [2,3]. However, PRES is seen in the absence of hypertension in 20–40% of patients and the reported BP usually does not reach the upper limit of autoregulation [2]. Furthermore, most imaging studies have revealed reduced rather than increased perfusion in the cerebral regions affected by PRES [2]. In the cytotoxic theory, hypertension is thought to lead to cerebral autoregulatory vasoconstriction, which worsens the existing systemic toxicity mediated by pro-inflammatory cytokines and endothelial dysfunction. The subsequent hypoperfusion leads to cerebral hypoxemia, which stimulates angiogenesis and increases endothelial permeability and capillary leakage, thus leading to vasogenic cerebral edema [4]. The high percentage of patients with PRES who have autoimmune disorders (45%) supports this theory [3]. Furthermore, pro-inflammatory cytokines are also involved in the pathogenesis of preeclampsia, which could explain its connection with PRES [4]. Regarding the connection between the two, PRES might be considered a rare complication of preeclampsia. PRES can be triggered by numerous conditions including eclampsia or preeclampsia, hypertension, renal failure, sepsis, auto-immune diseases, anticancer chemotherapy, immunosuppressive drugs and transplantation [1,2]. Thus, obstetricians have to intensify monitoring in women with severe, acute or atypical preeclampsia or in a context of high cardiovascular risk or autoimmunity. Headache, characterized by the occipital topography, is almost constant in PRES and can be associated with abnormalities of visual perception such as blurred vision, unilateral or bilateral cortical blindness or homonymous hemianopsia. Nausea, vomiting, mutism, stupor, confusion and generalized or partial seizures are also reported [1]. Deep tendon reflexes are classically brisk [1]. PRES in patients with preeclampsia, unlike PRES in patients with other conditions, often begins with mild symptoms, especially headache or visual disturbances [5]. Our cases highlight the fact that particular attention should be paid to these signs during pregnancy, peripartum or postpartum, because it can lead to an earlier diagnosis of PRES.

Differential diagnoses for PRES include stroke, cerebral venous thrombosis, encephalitis, demyelinating disorders and epilepsy, the latter being a major differential diagnosis that can delay the specific treatment of PRES, as in our second case. Cerebral vasoconstriction is mostly marked by recurrent thunderclap headaches and can be associated with PRES or isolated [6]. Actually, as the clinical symptoms of PRES are non-specific, diagnosis relies on neuroimaging [7]. CT/MR images of the brain typically show focal regions of hemispheric edema. The parieto-occipital regions are the most frequently affected; the frontal lobes, the inferior temporal-occipital junction, and the cerebellum are more rarely involved [2,4]. Typically, PRES predominantly affects subcortical (99%) and cortical (10%) white matter [3,7]. Imaging abnormalities tend to be symmetrical, but the degree of involvement and the clinical signs are often asymmetrical. There is no clear correlation between the clinical condition and specific imaging findings [3]. T2-weighted MRI shows areas of hyperintense signal [8]. For most patients, PRES can be diagnosed from CT-scan findings alone and the only advantage of MRI is that it may show small, focal abnormalities beyond the limit of resolution of a CT-scan [1]. Thus, CT-scan and CTA could be the first-line exams to rapidly rule out differential diagnoses. A subsequent MRI is necessary when the CT-scan is normal [2]. However, MRI Diffusion-Weighted Imaging (DWI) sequences and Apparent Diffusion Coefficient (ADC) mapping can be helpful to evaluate the prognosis because they can distinguish between areas of reversible vasogenic edema and areas of cytotoxic edema, which has potential long-term consequences [9]. High signal intensities on an ADC map suggest vasogenic edema, with a good prognosis, whereas a low ADC suggests foci of irreversible ischemia [10]. Early recognition of PRES is essential for the timely implementation of therapy, which typically consists of gradual BP control and the withdrawal of potential triggering agents [3]. In cases of preeclampsia, magnesium sulfate is useful to prevent seizures. According to some authors, nicardipine and labetalol are the first-line antihypertensive drugs. However, cerebral vasospasm can be treated, as in the three cases presented above, with nimodipine, which, unlike magnesium sulfate, is cerebral selective [8]. Interestingly, as some authors found PRES in almost all patients with eclampsia, they hypothesized that IV dexamethasone could be useful after an eclamptic seizure to reduce brain

edema [11]. Magnesium sulfate is classically used in cases of severe preeclampsia with neurological symptoms, but the efficacy of nimodipine or even dexamethasone to prevent PRES in preeclampsia should be prospectively evaluated. By definition, PRES is reversible, and on follow-up cerebral imaging, lesions have often resolved [2]. In rare cases, PRES can be complicated by status epilepticus, intracranial hemorrhage or massive cerebral ischemic infarction and thus lead to substantial morbidity and mortality [3]. Relapses have also been described [3]. Recently, a multidisciplinary model of risk factors was established and demonstrated that a low glucose level in the cerebrospinal fluid, hypertensive encephalopathy and imaging findings of hemorrhage were associated with increased mortality whereas preeclampsia was found to be protective [12].

In conclusion, the three cases and the short review of the literature highlight the particularly challenging diagnosis of PRES around pregnancy and its specific treatment.

Early diagnosis and prompt treatment are of paramount importance for a good prognosis. Thus, in patients presenting non-postural, severe headache, possibly accompanied by altered mental function and visual disturbance, PRES should be considered and treated without delay to maximize the potential for reversibility. The interest of preventive treatments in a context of preeclampsia with neurological symptoms should also be evaluated.

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