

Posterior reversible encephalopathy syndrome with reversible cerebral vasoconstriction syndrome in a normal primigravida woman at the 35-week gestational stage: a case report

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Background: Herein, we report a case of cerebral hemorrhage in a 21-year-old nulliparous, primi gravida woman caused by posterior reversible encephalopathy syndrome (PRES), which may be associated with reversible cerebral vasoconstriction syndrome (RCVS). **Case:** The patient's medical history was unremarkable, apart from the mother having had a cerebral infarction. She had been examined by a local doctor, and showed good progress; however, her blood pressure (BP) was 143/97 mmHg, she had findings of proteinuria (3+) and she had a headache on the 35th week with multiple vomiting episodes. She was admitted to our hospital after poor responsiveness and a consciousness level of GCS14, E4V4M6, a BP of 143/97 mmHg, a pulse rate of 77/min, bilateral abduction of the eyes, and left hemiplegia. Cranial computed tomography (CT) revealed cerebral hemorrhage with ventricular puncture in the right caudate nucleus. Emergency caesarean section was performed on the same day with priority given to maternal lifesaving. Acute cerebral infarction findings and PRES were observed on head magnetic resonance imaging (MRI) on the admission day 1. Head MR angiography on the 4th hospital day showed narrowing of the entire main artery trunk, suspected as RCVS. Short-term memory deficits were diagnosed post-extubation, but gradually improved. Although it became possible and hematoma in the ventricles were absorbed, left paresis and higher dysfunction were observed, and she was discharged on the 21st hospital day. **Conclusion:** PRES and RCVS occur simultaneously quite frequently, but require opposing treatment approaches. Both cases are reversible, but if they occur simultaneously, RCVS, which progresses slowly, may cause irreversible symptoms, thereby requiring careful treatment.

Keywords

Preeclampsia; Hypertensive crisis; Left hemiplegia; Posterior reversible encephalopathy syndrome; Reversible cerebral vasoconstriction syndrome

1. Introduction

Posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) are caused by vascular endothelial cell damage [1, 2]. They are also suspected to have common substrates and pathophysiologies. Additionally, as they are frequently associated with each other, both their diagnoses can be confirmed simultane-

ously through visual inspection. Here, we report a case of a primigravida woman with normal gestational course, until at 35 weeks when her pregnancy was complicated by PRES and RCVS.

2. Case presentation

The patient was a 21-year-old primigravida nullipara. Her medical and family history were unremarkable, apart from her mother's history of cerebral infarction. After a successful course of pregnancy, a local doctor examined her and noted that at 34 weeks of gestational age, her blood pressure (BP) was 131/97 mmHg, and the dipstick measure of proteinuria was 3+. During the 35th week, the patient experienced a sudden onset of a headache with excessive vomiting, upon which she was rushed to the hospital as she was barely responsive. On admission, her height (156 cm) and her weight (45 kg) were noted. Her weight before pregnancy was 38.5 kg. Her consciousness level of GCS14, E4V4M6,

BP was 143/97 mmHg, heart rate was 77 bpm, respiratory rate was 18 breaths/minute, and SpO₂ was 98%. There was no anisocoria, and the direct pupillary light reflex was normal; however, bilateral abduction of the eyes with left hemiplegia observed. Abdominal ultrasound showed no findings of premature separation of the placenta; fetal cardiotocography showed reassuring. Her white blood cell count (WBC) was 15,540/ μ L, hemoglobin (Hb): 9.2 g/dL, platelets: 21.9 \times 10,000/ μ L, liver enzymes serum aspartate aminotransferase (AST): 58 IU/L, serum alanine aminotransferase (ALT): 19 IU/L, lactate dehydrogenase (LDH): 342 U/L, blood urea nitrogen (BUN): 16.0 mg/dL, Creatinine: 0.89 mg/dL, total protein (TP): 4.2 g/dL, Albumin: 1.3 g/dL, Na: 139 mEq/L, K: 4.9 mEq/L, Cl: 110 mEq/L, CRP: 2.67 mg/dL. Proteinuria on dipstick urinalysis was 3+.

An area of high density was observed from the caudate nucleus to the lateral ventricles was noted on head CT. Areas of low density were also observed in the left basal ganglia, left putamen, bilateral occipital lobe, and the left parietal lobe (Fig. 1). The plain head MRI conducted on day 1,

including a diffusion-weighted MRI (DW-MRI) and ADC MRI, revealed an area of high density mainly in the occipital lobe, suggesting angioedema, which was diagnosed as PRES (Fig. 2).



Fig. 1. Head CT. There is a high absorption range from the caudate nucleus to the lateral ventricles; a low density area is observed in the right basal ganglia, left putamen, both occipital lobes, and left parietal lobe.

We suspected hemorrhage in the right caudate nucleus spreading into the ventricles, and multiple cerebral infarcts. Cardiogenic emboli, metastatic brain tumors, and Moyamoya disease were considered as differential diagnoses for the causes of multiple cerebral infarcts. A neurosurgeon consulted on the case, and there were no indications for urgent craniotomy or emergency ventricular drainage. Therefore, considering the gestational age and the future tests that would need contrast agents, we decided to follow a pregnancy-based plan.

Subsequently, her BP rose to 150/100 mmHg, so 1 mg of nicardipine hydrochloride was administered intravenously. This reduced the BP to 130/90 mmHg. During the surgery waiting time period, the patient's eyes turned upward, and tonic seizures were observed, requiring 5 mg diazepam to stop the seizure.

An emergency cesarean section was performed under general anesthesia lasting 2 h, 45 min after the headache occurred. A healthy baby boy weighing 2298 g was delivered via C-section. The Apgar Score was 8 at 1 min and 9 at 5 min.

The umbilical artery blood pH was 7.290. Blood loss was 999 ml (including volume of amniotic fluid), and the intraoperative BP was controlled at 100-120/50-70 mmHg. Postoperatively, nicardipine hydrochloride and diltiazem were administered for hypertension. Subsequently, we confirmed the disappearance of the high FLAIR signal in the same area (Fig. 2).

The Magnetic Resonance Angiography (MRA) conducted on day 1 revealed that the intracranial artery was diffusely stenotic and had infiltrated the peripheral artery. Suspecting RCVS, we started administering edaravone (a free radical scavenger).

On day 4, MRA revealed that an aggravated middle cerebral artery stenosis and the subsided peripheral arterial stenosis. A diagnosis of RCVS was confirmed. Subsequently, on days 16 and 34, cerebral vasospasm receded from the peripheral to the central portion. A thunderclap headache accompanied by an increase in BP was observed on day 2, but spontaneous remission occurred (Fig. 3). The patient was discharged from the hospital on day 21 with higher brain dysfunction and incomplete left paralysis (Figs. 4,5).

3. Discussion

PRES was first proposed by Hinchey in 1996 and was described as a condition encompassing headache, neurological disorders, convulsions, and visual impairment due to vasogenic cerebral edema (which mainly affects the white matter of the brain), caused by eclampsia or non-pregnancy-related hypertensive encephalopathy [1].

Regarding hypertension, in non-pregnant women, a rapid increase in BP is associated with organ damage such as those seen in hypertensive encephalopathy and stroke, defined as a hypertensive crisis [3]. Similarly, pregnancy-induced hypertensive nephropathy and hypertension could be accompanied by organ damage similar to that in eclampsia and stroke. Japanese clinical practice guidelines classify this as a hypertensive crisis too [4]. However, eclampsia may develop even when the BP is not as high as that in a non-pregnancy-induced hypertensive crisis [5]. The patient had a BP of 143/93 mmHg during delivery. In non-pregnant adults, this BP level will not induce a hypertensive crisis. Nevertheless, brain hemorrhage did occur, so it was suggested that the BP must have been even lower at the time of onset.

We speculatively associated this to existing vascular endothelial cell disease [6], given that pregnancy causes increased circulating blood cell counts, increased cardiac output, blood flow, and decreased vascular resistance and increased vascular permeability; blood flow particularly increases toward the uterus, placenta, and kidneys [6]. Conversely, cerebral circulation is maintained, as that during a non-pregnancy case, by controlling the reflux pressure through cerebral autoregulation in the vascular walls [6]. Cerebral autoregulation is controlled by neural and metabolic factors [7]. Regarding the neural factors, the cranial surface is controlled by the maxillary ganglia of the peripheral

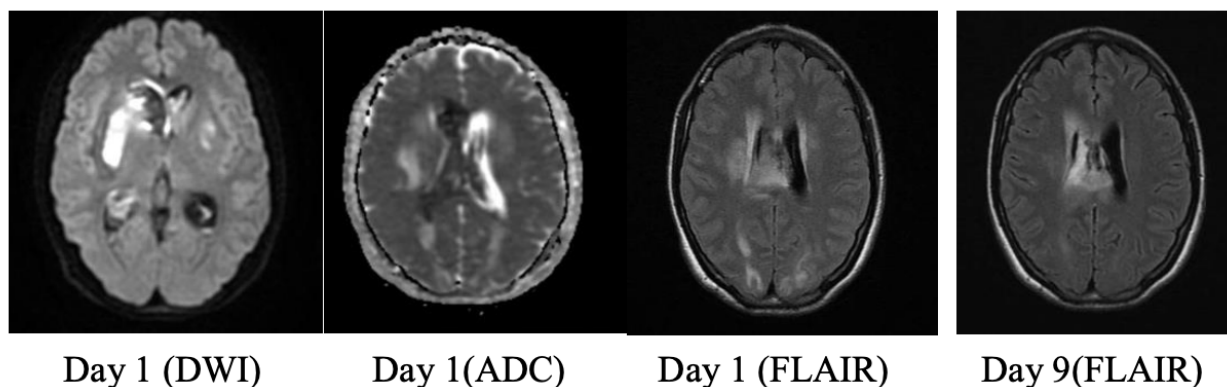


Fig. 2. Changes in PRES at MRI.

Day 1, DWI: No bilateral occipital lobe infarcts.

Day 1, ADC: An area of high density was observed in the occipital lobe, bilaterally.

Day 1, FLAIR: Hyperintensity was observed in the occipital lobe, bilaterally.

Day 9, FLAIR: There were findings of suspected vasogenic edema.

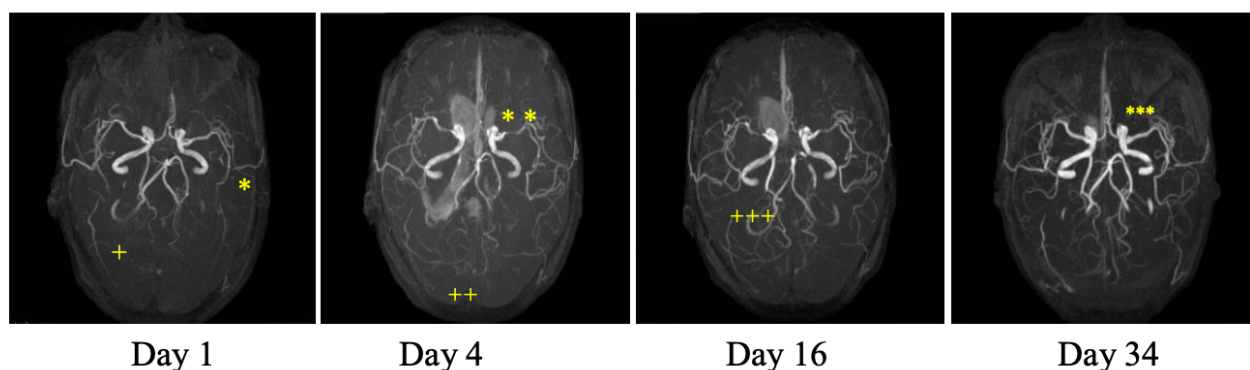


Fig. 3. Changes in RCVS at MRA.

On day 1, the intracranial artery was not visualized clearly*, and the peripheral artery had disappeared⁺, suggesting RCVS.

On day 4, stenosis was observed in the intracranial main artery**, and mild stenosis was observed in the peripheral artery⁺⁺. This was ruled as RCVS.

The peripheral arteries were further visualized on day 16⁺⁺⁺, and the stenosis of the main artery receded on day 34***.

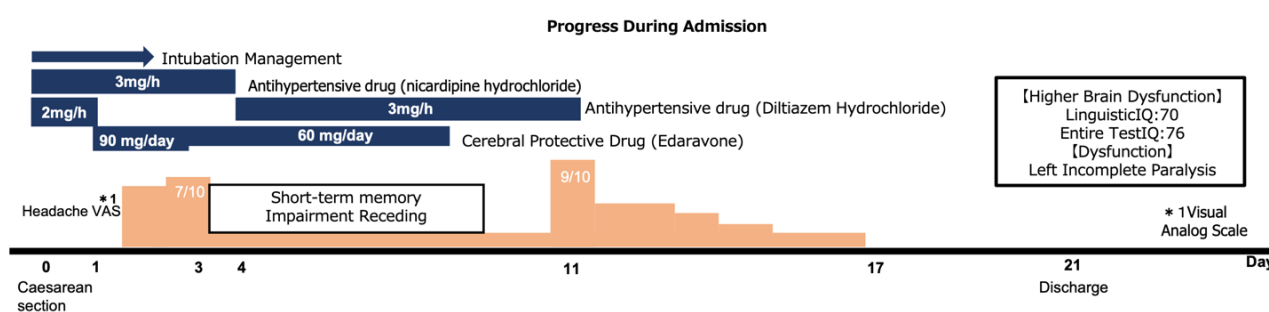


Fig. 4. Progress During Admission.

nerves, while the cranial parenchyma is governed by a nerve cluster (nucleus) of the central nervous system, which regulates blood flow using neurotransmitters released from its nerve fibers. However, the vasculature of the vertebral basilar artery and the occipital lobe has low sympathetic nerve density. Therefore, we surmised that the regulatory func-

tion failed due to a rapid increase in blood pressure. Consequently, vasogenic edema occurred in the white matter and stimulated seizures [8]. Therefore, we recommended lowering the BP to 140-159/90-109 mmHg with appropriate antihypertensive agents in addition to administering anticonvulsants during eclampsia [9-11].

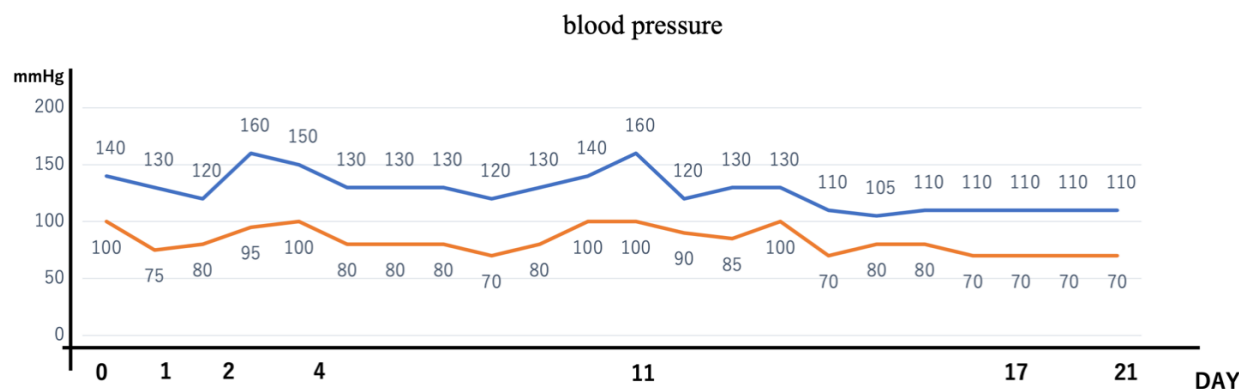


Fig. 5. Blood pressure.

RCVS was proposed by Calabrese *et al.* [11] in 2007, and described as a condition manifesting with thunderclap headache, vomiting, neurological deficits, and convulsions due to cerebral vasospasm. Blood vessels are believed to have non-injuries that are triggered by unspecified etiologies, which causes cerebral vasospasm and dilation. RCVS is often associated with cortical subarachnoid hemorrhage, but with unspecified etiology. Failure of the small arteries on the brain surface, or microleakage due to cerebral vasospasm, and reperfusion injury, are attributable causes of cerebrovascular endothelial dysfunction and failure of the blood-brain barrier [12].

In this case, the hemorrhage occurred in the right caudate nucleus, although it often accompanies subarachnoid hemorrhage (with an incidence rate reported as 30% to 45%), making it the most common complication. The diagnostic criteria for RCVS have not yet been established, but that proposed by Ducros in 2012 are useful [2].

Cerebral vasospasm needs to be confirmed by imaging, but, in most cases, RCVS cannot be confirmed by MRA within the first week of onset. Cerebral vasospasm reaches its peak at around 2 weeks after onset. Additionally, in the early stage, spasm begins from the arteriole; then, the stenosis of the main arteries around the circle of Willis is gradually observed [13].

Similar to this case, the MRA on day 1 revealed that spasms occurred mainly around the peripheral artery. However, from day 4 through 16, stenosis was observed in the main arteries.

A thunderclap headache occurs when the trigeminal nerves distributed in the cerebral blood vessels are stimulated by the spasm and expansion of the arterioles on the brain surface. In this case, a VAS 6-7/10 grade headache occurred on days 2 and 3, arterial spasm appeared simultaneously, and VAS 9/10 headache occurred on day 11. This gradually receded with the simultaneous dilation of arterioles [12].

At the time of cerebral vasospasm, the condition is similar to acute cerebral infarction; treatment is similar to that for acute cerebral infarction and is considered necessary. Although thrombolysis was not required in this case, the neu-

rons were exposed to oxidative stress; edaravone was administered.

Edaravone is a free radical scavenger that is thought to reduce oxidative stress which has been implicated in neuronal cell death in stroke. Edaravone is a drug with potential neuroprotective properties for acute brain infarction according to the Japanese Guidelines for the Management of Stroke, and its use is recommended.

There have been several reports on the relationship between eclampsia and the concurrence of PRES and RCVS.

Complication rate of PRES in patients with eclampsia has been reported to be 92–97%. Posterior reversible cerebral edema seen in PRES was found in 9–38% of patients with RCVS, and cerebral vasospasm seen in RCVS was found in more than 85% of patients with PRES. A total of 9% of cases of PRES were reported to occur during the puerperium, but it is thought to have occurred before childbirth in this case. A total of 1–13% of cases of RCVS and 92% of cases of RCVS occur during the puerperium [14–16]. Therefore, this case is considered important because the patient had both PRES and RCVS during pregnancy, but they were difficult to diagnose during the initial response, because the symptoms of RCVS appeared late.

With respect to PRES, antihypertensive therapy is the main option for managing hypertensive emergencies; a systolic blood pressure lower than 140 mmHg or a mean arterial pressure lower than 110 mmHg is recommended for cerebral hemorrhage. However, in the case of RCVS, antihypertensive therapy may lead to a decrease in peripheral blood flow which may contribute to cerebral ischemia, since cerebral vasoconstriction may reduce cerebral blood flow. Furthermore, one study reported the possibility of persistent pituitary damage from a peripartum non-hemorrhagic, vasoconstriction event [17]. In this case, antihypertensive treatment for intracerebral hemorrhage and diazepam therapy for treatment of seizures were administered, since the patient was already suffering from impaired consciousness due to cerebral hemorrhage, but careful treatment planning is required for each case.

4. Conclusion

PRES and RCVS occur simultaneously quite frequently, but require opposing treatment approaches. Both cases are reversible, but if they occur simultaneously, RCVS, which progresses slowly, may cause irreversible symptoms, thereby requiring careful treatment.

Author contributions

ST, MG, SW, SK, SH, SF, MO, LL, YT, SN, FE and HT provided help and advice on this case report. All authors approved the final report.

Ethics approval and consent to participate

The case report was approved by the ethic committee of Iizuka Hospital (2019000466). This patient gave their informed consent they participated in the case report.

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Conflict of interest

The authors declare no conflict of interest.

References

- [1] Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior leukoencephalopathy syndrome. *New England Journal of Medicine*. 1996; 334: 494–500.
- [2] Ducros A. Reversible cerebral vasoconstriction syndrome. *Lancet Neurology*. 2012; 11: 906–917.
- [3] Umemura S, Arima H, Arima S, Asayama K, Dohi Y, Hirooka Y, et al. The Japanese Society of Hypertension guidelines for the management of hypertension (JSH 2019). *Hypertension Research*. 2019; 42: 1235–1481.
- [4] Minakami H, Maeda T, Fujii T, Hamada H, Iitsuka Y, Itakura A, et al. Guidelines for obstetrical practice in Japan: Japan Society of Obstetrics and Gynecology (JSOG) and Japan Association of Obstetricians and Gynecologists (JAOG) 2014 edition. *Journal of Obstetrics and Gynaecology Research*. 2014; 40: 1469–1499.
- [5] Too GT, Hill JB. Hypertensive crisis during pregnancy and postpartum period. *Seminars in Perinatology*. 2013; 37: 280–287.
- [6] Schwartz RB, Feske SK, Polak JF, DeGirolami U, Iaia A, Beckner KM, et al. Preeclampsia-eclampsia: clinical and neuroradiographic correlates and insights into the pathogenesis of hypertensive encephalopathy. *Radiology*. 2000; 217: 371–376.
- [7] *Obstetrics and Gynecology Treatment*. 2010; 100: 1074–1084.
- [8] Wiegman MJ. Maternal brain involvement in (pre) eclampsia. Pathophysiology and long-term consequences [PhD dissertation]. University of Groningen. 2012.
- [9] Committee on Obstetric Practice. Committee Opinion No. 514: emergent therapy for acute-onset, severe hypertension with preeclampsia or eclampsia. *Obstetrics and Gynecology*. 2011; 118: 1465–1468.
- [10] Committee on Obstetric Practice. Committee Opinion No. 263: emergent therapy for acute-onset, severe hypertension with preeclampsia or eclampsia. *Obstetrics and Gynecology*. 2015; 125: 521–525.
- [11] Committee on Obstetric Practice. Committee Opinion no. 692: emergent therapy for acute-onset, severe hypertension during pregnancy and the postpartum period. *Obstetrics and Gynecology*. 2017; 129: e90–e95.
- [12] Calabrese LH, Dodick DW, Schwedt TJ, Singhal AB. Narrative review: reversible cerebral vasoconstriction syndromes. *Annals of Internal Medicine*. 2007; 146: 34–44.
- [13] Ducros A, Boukobza M, Porcher R, Sarov M, Valade D, Bousser M. The clinical and radiological spectrum of reversible cerebral vasoconstriction syndrome. A prospective series of 67 patients. *Brain*. 2007; 130: 3091–3101.
- [14] Singhal AB, Hajj-Ali RA, Topcuoglu MA, Fok J, Bena J, Yang D, et al. Reversible cerebral vasoconstriction syndromes: analysis of 139 cases. *Archives of Neurology*. 2011; 68: 1005–1012.
- [15] Ducros A, Fiedler U, Porcher R, Boukobza M, Stapf C, Bousser MG. Hemorrhagic manifestations of reversible cerebral vasoconstriction syndrome: frequency, features, and risk factors. *Stroke*. 2010; 41: 2505–2511.
- [16] Chen S, Fuh J, Wang S, Chang F, Lirng J, Fang Y, et al. Magnetic resonance angiography in reversible cerebral vasoconstriction syndromes. *Annals of Neurology*. 2010; 67: 648–656.
- [17] Kuriya A, Morris DV, Dahan MH. Pituitary injury and persistent hypofunction resulting from a peripartum non-hemorrhagic, vaso-occlusive event. *Endocrinology, Diabetes & Metabolism Case Reports*. 2015; 2015: 150001.