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CLINICAL REPORT

A case of posterior reversible encephalopathy syndrome after emergence from anesthesia

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Abstract Posterior reversible encephalopathy syndrome (PRES) is a relatively new clinical entity characterized by reversible neurological symptoms with findings indicating leukoencephalopathy on imaging studies. Reports of PRES in the field of anesthesiology have been quite limited. A patient with therapeutic anticoagulant developed PRES immediately after emergence from anesthesia, in which her status was initially recognized as delayed recovery from anesthesia with transient hypertension because an emergent head computed tomography (CT) scan was almost normal. Subsequently, magnetic resonance imaging (MRI) was also performed according to a radiologist's recommendation because the CT results showed areas of slightly low attenuation in the frontoparieto-occipital lobes bilaterally, suggesting PRES; otherwise, ischemic events. MRI showed subcortical increased T_2 and fluid-attenuated inversion recovery (FLAIR) intensity in the occipitoparietal regions bilaterally with slight increase in the apparent diffusion coefficient signal on diffusion-weighted imaging, which confirmed a diagnosis of PRES. Gradually, the patient regained consciousness and became responsive with antihypertensive therapy. A prompt and accurate diagnosis of PRES is important to avoid irreversible brain damage, for example, intracranial hemorrhage, especially in a patient receiving anticoagulation therapy.

Keywords Posterior reversible encephalopathy syndrome · Ketamine · Anticoagulation · Hypercapnia · Hypertension

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Introduction

As described by Hinchey and colleagues [1], reversible posterior leukoencephalopathy syndrome, in which posterior reversible encephalopathy syndrome (PRES) is now more usually used to described to this syndrome, is a relatively new clinical entity characterized by a reversible syndrome of headache, altered mental functioning, seizures, and loss of vision associated with findings indicating predominantly posterior leukoencephalopathy on imaging studies [2]. PRES is classically characterized as symmetrical parieto-occipital edema but may occur in other distributions with varying imaging appearances [3]. One of the distinctive characteristics of PRES is the reversibility of the clinical and radiologic abnormalities after appropriate treatment and removal of the precipitating factors [1, 4]. As one of the interesting examples of PRES during perioperative periods, reversible postoperative blindness, which was successfully treated by early accurate diagnosis and appropriate blood pressure control, has been reported to be associated with PRES [5].

We describe a patient with therapeutic anticoagulant who developed PRES immediately after emergence from anesthesia, in which her status was initially recognized as delayed recovery from anesthesia because an emergent head computed tomography (CT) scan was almost normal.

Case report

Institutional Review Board approval and informed consent were exempted because no ethical problem was included in this case report, and the patient cannot be identified from case presentation alone, although the patient's consent for publication had been obtained. A 67-year-old female

patient was admitted to hospital for an exploratory laparotomy because of suspicion of ovarian cancer. Her medical history included essential hypertension treated with benidipine (Ca channel blocker), paroximal atrial fibrillation treated with cibenzoline (Na channel blocker) and warfarin, symptomatic deep venous thrombosis (DVT) treated with warfarin, and mild aortic valve stenosis (pressure gradient = 30 mmHg). On admission, her weight was 47 kg and her height was 1.58 m. Her blood count revealed anemia (hemoglobin, 9.6 g/dl), and her blood pressure (BP) was 160/90 mmHg. After admission, her BP was fluctuated between 160/100 and 120/70. Otherwise, her physical examination and tests, including blood electrolytes, renal and liver function tests, electrocardiogram, and pulmonary function tests, were normal. In addition, she had no neurological deficits. Three days before the surgery, therapeutic anticoagulation was switched from warfarin to continuous heparin infusion (500–700 U/h). On the day of the surgery, the patient received no premedication. In the operating room, the patient was monitored with electrocardiogram, noninvasive arterial blood pressure, and pulse oximetry. Her arterial blood pressure was 180/100 and heart rate was 70 bpm. General anesthesia was induced using propofol 50 mg, ketamine 50 mg, and fentanyl 0.1 mg IV; muscle relaxation was achieved with rocuronium 30 mg. The i-gel #3 (Intersurgical Ltd, Wokingham, Berkshire, UK) was inserted, and her lungs were mechanically ventilated with 40% oxygen. Ventilation was adjusted to maintain $EtCO_2$ at 30–35 mmHg. Anesthesia was maintained with 1.3% sevoflurane and continuous infusion of remifentanil 0.15 μg/kg/h, and intermittent doses of fentanyl (0.2 mg). Ketamine 40 mg was also administered during anesthesia. The operation was uneventful and lasted 1 h and 15 min; the patient was stable, and intraoperative BP was 165/90 after the i-gel insertion. Other intraoperative BP was maintained at 110–130/60–70 mmHg. At the end of surgery, muscle relaxation was reversed with sugammadex 100 mg. She opened her eyes and responded to verbal commands, although she was not alert, in which she seemed to be typically affected by ketamine. $EtCO_2$ under spontaneous breathing was around 50 mmHg with respiratory rate 12–15/min and tidal volume 300–330 ml. The i-gel was removed when her BP was 155/85 mmHg. During the next few minutes she was stable; however, her BP gradually increased to 220/120 mmHg. Simultaneously, she showed no response to stimuli and started shivering. Bolus doses of nicardipine 2 mg, diltiazem 10 mg, and landiolol (ultra-short-acting beta-blocker) 20 mg were administered to stabilize her BP. Approximately 10 min later, her BP decreased to 160/90 mmHg. Her pupils were 2.5 mm in each eye and reactive to light. However, she was still unconscious and shivering although she was breathing stably. We were concerned that she had developed intracranial hemorrhage and decided to perform an emergent head CT scan. The results were almost normal; at least, hemorrhage was not observed. Based on the CT results, she was transferred to the postsurgical care units and observed with a diagnosis of prolonged recovery from anesthesia. Her BP was controlled around 150 mmHg by continuous infusion of nicardipine. She stopped shivering but was still unconscious. Soon after, a senior radiologist who happened to see the CT results recommended a further magnetic resonance imaging (MRI) examination because the CT results showed areas of slightly low attenuation in the frontoparieto-occipital lobes bilaterally, suggesting PRES; otherwise, the clinical features did not deny global infarct or ischemia in the very early stage (Fig. 1a). MRI was performed to distinguish PRES from acute cerebral infarction when 2 h had passed since the end of the surgery. It showed subcortical increased T_2 and fluid-attenuated inversion recovery (FLAIR) intensity in the occipito-parietal regions bilaterally (Fig. 1b) with slight increase in the apparent diffusion coefficient signal (ADC) on diffusion-weighted

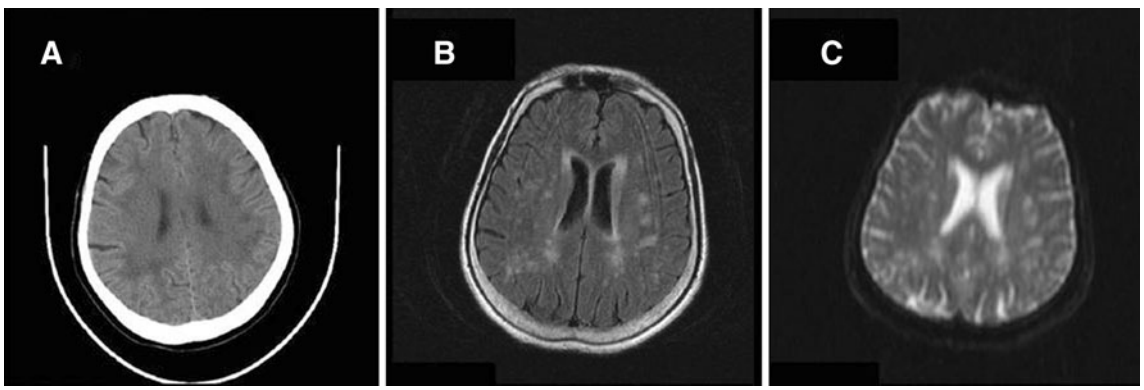

Fig. 1 **a** Slightly low attenuation in head computed tomography seen in the frontoparieto-occipital lobes bilaterally. **b** Subcortical increased fluid-attenuated inversion recovery intensity seen in the occipito-parietal regions bilaterally. **c** Slight increase in the apparent diffusion coefficient signal on diffusion-weighted imaging

imaging (DWI) (Fig. 1c). The abnormal area in the MRI appeared to be smaller than expected based on the CT results. When the clinical features were also taken into account, these imaging findings suggested a diagnosis of PRES. In the postsurgical care unit, nicardipine infusion was continued to maintain a systolic BP <130 mmHg. Gradually, the patient regained consciousness and became responsive. Six hours later, the patient recovered fully and was oriented and coherent with no neurological deficit. She was no longer symptomatic.

Discussion

According to typical reversible clinical symptoms and neuroimaiging findings in this patient, it can be safely said that this was PRES with the hypertensive episode as a trigger [1–4]. Retrospectively, the observed shivering after anesthesia might be a kind of myoclonic seizure caused by PRES. The underlying pathophysiology of PRES remains not fully understood. Of several theories that have been proposed previously, the currently favored hypothesis is that rapidly developing hypertension leads to a breakdown in cerebral autoregulation and the blood–brain barrier, cerebral vasodilatation, and transudation of fluid, resulting in brain edema [1, 6]. However, PRES in the absence of severe hypertension can also occur, in which it has been proposed that the presence of some specific medical conditions, for example, eclampsia or immunosuppressive therapy, are likely predominantly related to blood–brain barrier disruption or may affect vasomotor tone [7]. In our case, several agents used intraoperatively or the pathophysiological status immediately after recovery from anesthesia might be related to development of PRES as well as the transient hypertensive episode because she had experienced the same degree of hypertension previously.

The timing when PRES happened in this case is supposed to have been after recovery from anesthesia, but not during anesthesia, because she was responsive immediately after emergence. Just before removal of the i-gel, her $EtCO_2$ was around 50 mmHg. It has been reported that cerebrovascular carbon dioxide reactivity is preserved in hypertensive patients [8]. Therefore, cerebral blood flow (CBF) was modestly increased at that time. The objection will no doubt be raised that 50 mmHg $PaCO_2$ does not seem to have significant effect on CBF. However, it is true that CBF increases in proportion to $PaCO_2$. Therefore, CBF truly increased around the end of anesthesia. In addition, ketamine was used intraoperatively in this case to prevent remifentanil-induced postoperative hyperalgesia [9]. She was responsive; however, she seemed to be typically affected by residual ketamine. It has been also reported that ketamine, even subanesthetic doses of ketamine, induces increase in CBF [10]. The effect of ketamine on CBF can be affected by concomitant use of other anesthetics. Intraoperatively, she received propofol, sevoflurane, and fentanyl. However, propofol was only used at induction of anesthesia. The expiratory concentration of sevoflurane was almost zero just before extubation. It has been reported that CBF did not change with moderate doses of fentanyl (25 μg/kg) [11]. Therefore, immediately after extubation, it is reasonable to suppose that her cerebral hemodynamics was not affected by residual fentanyl. It is likely that residual ketamine partially contributed to increase CBF postoperatively. As causal episodes of PRES, we can see reports suggesting that general anesthesia might be associated with PRES by precipitating complications of cytotoxic or immunosuppressant therapy, although its mechanisms was not referred to clearly [7]. Thus, the combination of hypercapnia and residual ketamine in addition to perioperative poor BP control might contribute to development of PRES in this patient, although there is no doubt that the hypertensive episode essentially contributed to development of PRES. It is reasonable to propose that fluctuations in BP during perioperative periods should be avoided, especially in poor controlled hypertensive patients, because postoperative hypercapnia and residual anesthetics immediately after emergence are very likely. The possibility that other factors might be responsible should also be considered. Changes in serum electrolytes or albumin during anesthesia might induce PRES in a susceptible brain [12]. However, it is not determined whether these contributed to develop PRES in this patient because they were not measured at that time. As an appended concern, it cannot be denied that remifentanil withdrawal hyperalgesia contributed to the hypertensive episode, which was mostly related to development of PRES in this case, although we intended to prevent development of this hyperalgesia with ketamine [13].

Early recognition of PRES is important for timely institution of therapy, which typically consists of gradual blood pressure control and withdrawal of potentially offending agents. Distinguishing between thrombotic or embolic stroke and hemorrhagic stroke is paramount when considering treatment of arterial blood pressure. Especially, she had both risks because of paroxysmal atrial fibrillation and concomitant heparin infusion. To make the diagnosis, an emergent CT may be helpful. However, the accurate diagnosis for PRES is also important. Delayed diagnosis can lead to severe and long-term neurological disability [1, 4]. It has been suggested that the term PRES is a misnomer as the condition is not always reversible [14]. Indeed, intracranial hemorrhage is known to occur following PRES [15]. Specific conditions, for instance, therapeutic anticoagulation, can increase the rate of intracranial hemorrhage in PRES [15]. Radiographically, PRES

manifests on CT as hypodensities of the posterior white and gray matter. Lesions are generally bilateral and parieto-occipital, but may involve temporal or frontal lobes, brainstem, or cerebellum. However, CT scanning is less sensitive; thus, MRI is the favored modality of investigation [16]. T_2-weighted MRI and FLAIR sequences show areas of hyperintense signal. DWI may help distinguish vasogenic edema (increased ADC) from cytotoxic edema (reduced ADC, seen in acute arterial ischemic injury) [7]. Taking her complicated medical condition into account, a subsequent MRI based on the radiologist's recommendation was helpful for the following appropriate treatment of PRES.

Conclusion

We presented a patient who developed PRES immediately after emergence from anesthesia. Residual anesthetics and hypercapnia as well as a transient hypertensive episode were presumed to be possible causal factors of PRES. A prompt and accurate diagnosis of PRES is important to avoid irreversible brain damage, for example, intracranial hemorrhage, especially in a patient receiving anticoagulation therapy.

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References

1. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, Pessin MS, Lamy C, Mas JL, Caplan LR. A reversible posterior leukoencephalopathy syndrome. N Engl J Med. 1996; 334:494–500.
2. Casey SO, Sampaio RC, Michel E, Truwit CL. Posterior reversible encephalopathy syndrome: utility of fluid-attenuated inversion recovery MR imaging in the detection of cortical and subcortical lesions. AJNR Am J Neuroradiol. 2000;21:1199–206.
3. McKinney AM, Short J, Truwit CL, McKinney ZJ, Kozak OS, SantaCruz KS, Teksam M. Posterior reversible encephalopathy syndrome: incidence of atypical regions of involvement and imaging findings. AJR Am J Roentgenol. 2007;189:904–12.
4. Kwon S, Jahoon K, Sangkwon L. Clinical spectrum of reversible posterior leukoencephalopathy syndrome. Pediatr Neurol. 2001; 24:361–64.
5. Kim TK, Yoon JU, Park SC, Lee HJ, Kim WS, Yoon JY. Postoperative blindness associated with posterior reversible encephalopathy syndrome: a case report. J Anesth. 2010;24:783–5.
6. Schwartz RB, Jones KM, Kalina P, Bajakian RL, Mantello MT, Garada B, Holman BL. Hypertensive encephalopathy: findings on CT, MR imaging, and SPECT imaging in 14 cases. AJR Am J Roentgenol. 1992;159:379–83.
7. Rangi PS, Partridge WJ, Newlands ES, Waldman AD. Posterior reversible encephalopathy syndrome: a possible late interaction between cytotoxic agents and general anaesthesia. Neuroradiology. 2005;47:586–90.
8. Tominaga S, Strandgaard S, Uemura K, Ito K, Kutsuzawa T. Cerebrovascular CO_2 reactivity in normotensive and hypertensive man. Stroke. 1976;7:507–10.
9. Joly V, Richebe P, Guignard B, Fletcher D, Maurette P, Sessler DI, Chauvin M. Remifentanil-induced postoperative hyperalgesia and its prevention with small-dose ketamine. Anesthesiology. 2005;103:147–55.
10. Långsjö JW, Kaisti KK, Aalto S, Hinkka S, Aantaa R, Oikonen V, Sipilä H, Kurki T, Silvanto M, Scheinin H. Effects of subanesthetic doses of ketamine on regional cerebral blood flow, oxygen consumption, and blood volume in humans. Anesthesiology. 2003;99:614–23.
11. Hänel F, Werner C, von Knobelsdorff G, Schulte am Esch J. The effects of fentanyl and sufentanil on cerebral hemodynamics. J Neurosurg Anesthesiol. 1997;9:223–7.
12. Pirker A, Kramer L, Voller B, Loader B, Auff E, Prayer D. Type of edema in posterior reversible encephalopathy syndrome depends on serum albumin levels: an MR imaging study in 28 patients. AJNR Am J Neuroradiol. 2011;32:527–31.
13. Engelhardt T, Zaarour C, Naser B, Pehora C, de Ruiter J, Howard A, Crawford MW. Intraoperative low-dose ketamine does not prevent a remifentanil-induced increase in morphine requirement after pediatric scoliosis surgery. Anesth Analg. 2008;107:1170–5.
14. Stott VL, Hurrell MA, Anderson TJ. Reversible posterior leukoencephalopathy syndrome: a misnomer reviewed. Intern Med J. 2005;35:83–90.
15. Hefzy HM, Bartynski WS, Boardman JF, Lacomis D. Hemorrhage in posterior reversible encephalopathy syndrome: imaging and clinical features. AJNR Am J Neuroradiol. 2009;30:1371–9.
16. Mukherjee P, McKinstry RC. Reversible posterior leukoencephalopathy syndrome: evaluation with diffusion-tensor MR imaging. Radiology. 2001;219:756–65.