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CLINICAL REPORT

A case of delayed emergence from anesthesia caused by postoperative brain edema associated with unexpected cerebral venous sinus thrombosis

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Abstract Cerebral venous sinus thrombosis (CVST) is rare but displays various and often dramatic clinical symptoms. Few cases of CVST have been reported in the field of anesthesiology. We encountered an unexpected case of CVST that presented with delayed emergence from anesthesia after resection of a brain tumor. A 55-year-old man was scheduled for resection of an oligoastrocytoma in his right frontal lobe. After smooth induction of general anesthesia, anesthesia was maintained uneventfully for about 7 h with target-controlled infusion (TCI) of propofol and remifentanil, except for a seizure generated when the right anterior central gyrus was stimulated to allow motor evoked potential monitoring. Immediately after the cessation of TCI, spontaneous respiration was restored. However, the patient was unexpectedly comatose, and no response to painful stimuli or coughing during tracheal suctioning was observed. A computed tomogram taken 2 h after surgery showed diffuse brain edema, even though the neurosurgeons did not notice any cerebral swelling during closing of the dura mater. A magnetic resonance venogram revealed thromboses in the superior sagittal and straight sinuses. On the 9th postoperative day, the patient died without recovering consciousness or his brainstem reflexes. Anesthesiologists should be aware of CVST as a cause of delayed emergence from anesthesia after craniotomy.

Keywords Delayed emergence from anesthesia · Cerebral venous sinus thrombosis · Brain edema Hypoxic-ischemic encephalopathy · Craniotomy

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Introduction

Cerebral venous sinus thrombosis (CVST) is an uncommon but clinically important condition with an estimated annual incidence of 3 to 4 cases per million in adults. It is being diagnosed more frequently than in the past because of improvements in diagnostic imaging techniques [1–3]. However, to the best of our knowledge, there are no reports about cases of CVST involving anesthesia. Here, we describe a neurosurgical case of delayed emergence from anesthesia caused by CVST, which resulted in death from serious brain edema.

Case description

A 55-year-old man (height 164 cm, weight 46 kg) had suffered an epileptic seizure 6 years previously. Computed tomography (CT) and magnetic resonance imaging (MRI) had revealed a brain tumor in his right frontal lobe, which had been resected and diagnosed as oligoastrocytoma. Since then, under temporary chemotherapy and radiotherapy, he had been prescribed anticonvulsants (phenobarbital, phenytoin, and zonisamide) to prevent seizures. Nevertheless, he had suffered repetitive epileptic seizures once every few months. Furthermore, the recent MRI detected a mass lesion in the right frontal lobe (Fig. 1). Thus, he was scheduled to undergo resection of the recurrent brain tumor.

Preoperatively, the patient displayed normal findings on physical and laboratory examinations. No premedication was given. Under standard monitoring, anesthesia was induced with intravenous propofol (80 mg), the trachea was intubated using rocuronium (40 mg), and the lungs were mechanically ventilated with 50–60 % oxygen in air.

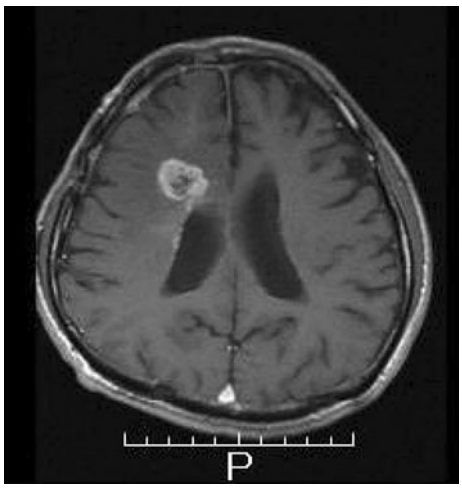

Fig. 1 A mass lesion was observed in the right frontal lobe on preoperative T_1 magnetic resonance imaging

To monitor the motor evoked potentials (MEP), the effect of rocuronium was reversed with 100 mg sugammadex after tracheal intubation. A single seizure was generated in the left arm when the right anterior central gyrus was stimulated for MEP monitoring, despite preventive administration of fosphenytoin (750 mg) during opening of the dura mater. Propofol (20 mg) and fosphenytoin (750 mg) were immediately given, resulting in abrogation of the seizure. An additional 750 mg fosphenytoin was administered before the dura mater was closed. The anesthesia was otherwise uneventful, although the patient was slightly hypothermic [rectal temperature (RT), 35.1–35.7 °C], and was maintained via target-controlled infusion (TCI) of propofol (effect compartment concentration, 3.0 ± 0.5 μg/ml) combined with the continuous infusion of remifentanil at 0.25 μg/kg/min and administration of 100 μg fentanyl at the end of the procedure. The surgery lasted 6 h, and no brain swelling was noted by the neurosurgeons when closing the dura mater. Total blood loss, urine output, and volume of crystalloid solution transfused were 230 g, 2,400 ml, and 3,850 ml (including 200 ml 15 w/v% D-mannitol), respectively.

Immediately following the cessation of TCI, spontaneous breathing was restored (respiratory rate, 8 breaths/min; end-tidal CO_2, 45 mmHg; tidal volume, 400 ml). However, he exhibited a comatose level of consciousness, was unresponsive to painful stimuli, and did not cough during tracheal suctioning, with RT of 35.7 °C. Both his pupils were 2 mm in diameter and thus too small to allow us to judge their light reflexes. Initially, we considered that the intraoperative fosphenytoin, anesthetic agents, and mild hypothermia might have been responsible for the patient's delayed emergence from anesthesia. An hour after the end of the procedure, the patient's consciousness had not improved, and he was transferred to the recovery room while still under tracheal intubation with no sedatives and was managed under synchronized intermittent mandatory ventilation with an F_IO_2 of 0.5–0.6. The patient's postoperative laboratory data were all within normal limits. One hour later, as he was still comatose, a head CT scan was performed that revealed diffuse brain edema (Fig. 2a). At that time, his isochoric pupils were dilated to 9 mm in diameter and did not display light reflexes, and he had no brainstem reflexes, indicative of a score of 300 on the Japan Coma Scale. Two hours after the CT scan, a further MRI examination was performed to investigate the cause of the patient's coma. Trans-axial T_2-weighted gradient-echo and fluid-attenuated inversion recovery (FLAIR) MRI showed extensive confluent areas of high signal intensity in the cerebral white matter and bilateral areas of the basal ganglia. Abnormally high signal intensity was also observed in the bilateral areas of the basal ganglia on diffusion-weighted MRI (Fig. 2b). Moreover, CVST was detected in the superior sagittal and straight sinuses on a magnetic resonance venogram and dynamic gadolinium-enhanced MRI sequences (Fig. 2c), suggestive of serious hypoxic-ischemic encephalopathy in association with CVST. As the extensive brain edema was unresponsive to head elevation and mannitol infusion, it was considered that aggressive treatment with thrombolysis, anticoagulation with heparin, or decompressive craniotomy would have been ineffective. Finally, he died on the 9th postoperative day.

Discussion

Failure to awake from a neurosurgical procedure can be disconcerting and multifactorial in nature. Delayed emergence from anesthesia, which is sometimes defined as difficulty with arousal that lasts for more than 15 min after the cessation of anesthesia [4], can be attributed to several etiological factors, e.g., anesthetic agents; hypothermia; abnormal glucose, electrolyte, and arterial blood gas (hypoxemia and/or hypercarbia) levels; various psychoactive substances; relatively large brain tumors; relatively large areas of the brain being traumatized by surgery; or epilepsy [5–7]. With regard to the present case, we initially considered that the transitory residual effects of fosphenytoin, fentanyl, and propofol and/or the mild hypothermia suffered by the patient had caused the patient's delayed emergence from anesthesia. However, the subsequent coma prompted us to perform diagnostic imaging, which revealed unanticipated brain edema and cerebral vein thromboses in the superior sagittal and straight sinuses, resulting in the patient's death. To the best of our knowledge, there are no published reports about delayed emergence from anesthesia caused by hypoxic-ischemic

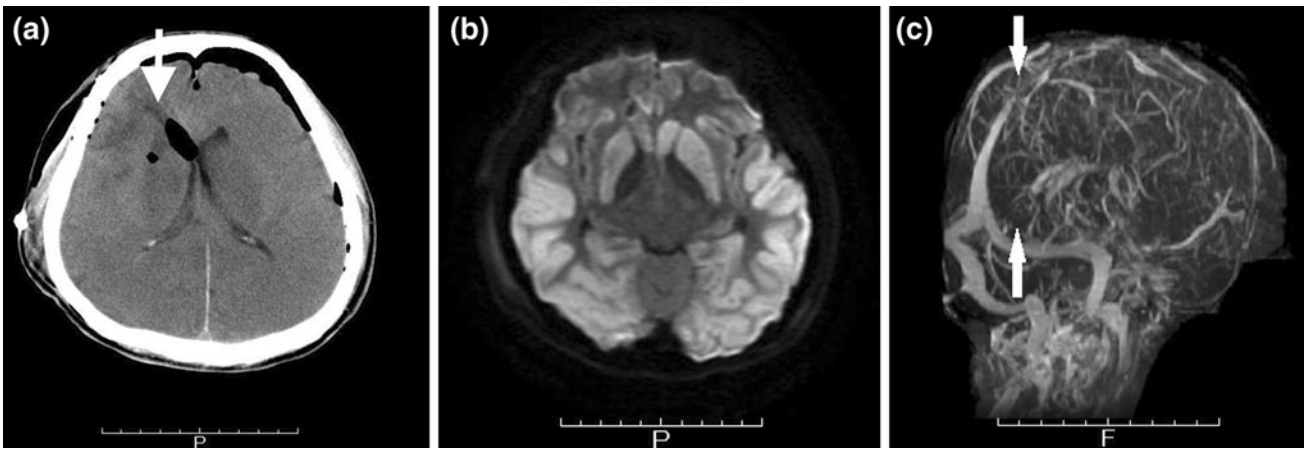

Fig. 2 **a** Diffuse brain swelling and the resection site of the brain (*arrow*) were observed on a computed tomogram. **b** Bilateral areas of the basal ganglia displayed abnormally high signal intensity on diffusion-weighted magnetic resonance images. **c** *Arrows* show a dural (superior sagittal and straight) sinus thrombosis on an oblique view magnetic resonance venogram

encephalopathy associated with CVST in the absence of intraoperative incidents.

CVST is an uncommon condition with various and often dramatic clinical symptoms. The most frequent thrombus locations are the superior sagittal (60 %) and transverse sinuses (40–50 %), but more than one sinus is involved in two thirds of cases [3]. The mechanisms of CVST remain unclear, and the following risk factors are considered to be involved: (1) local factors: head injury, craniotomy, meningitis, cerebral arteriovenous malformation, and brain tumor; (2) systemic factors: dehydration, pregnancy, inflammatory bowel disease, malignancy, and sarcoidosis; (3) drugs: oral contraceptives and androgens; and (4) blood dyscrasias: leukemia and thrombocythemia [1, 3, 8, 9]. However, even after extensive investigation, no cause is identified in 20–25 % of cases [9]. Because of the wide spectrum of clinical features displayed by CVST and the varying speed of their onset, CVST is frequently overlooked or its diagnosis is delayed. The symptoms of CVST vary and depend on the venous structures involved. The most common symptoms are headache and papilledema caused by intracranial hypertension, seizures, focal neurological deficits, and altered consciousness [1]. In addition, approximately 30–40 % of patients with CVST present with intracerebral hemorrhage [10]. In patients with such clinical features, imaging of the cerebral venous system (CT venography, MRV) is reasonable to exclude CVST. It is reported that the symptoms of CVST display a subacute onset, taking from 2 days to 1 month to develop in 50–80 % of patients and even longer in 10–20 % of patients. The prognosis is favorable in more than 80 % of cases; on the other hand, a poor neurological outcome is seen in 7–20 % of cases [10–12]. In our case, the patient had few risk factors for CVST but had suffered a seizure and undergone craniotomy for a brain tumor. However, these events are so common that we could not ultimately clarify the pathogenesis and cause of the critical CVST, which triggered brain edema, hypoxic-ischemic encephalopathy, and eventually death.

According to a proposed algorithm for the management of CVST, all patients diagnosed as CVST confirmed by imaging require initiation of anticoagulation. In addition, decompressive hemicraniectomy or endovascular therapy should be taken into consideration in patients having neurological deterioration or coma despite medical treatment. However, the algorithm is neither comprehensive nor applicable to all clinical scenarios, and patient management must be individualized [13].

We reported a case of unexpected CVST, which suggests that anesthesiologists should be aware of CVST as a cause of delayed emergence from anesthesia after craniotomy

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