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Case Report

One case with dexmedetomidine-induced stuporous state in epileptic patient undergoing abdominal surgery

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Abstract: A 56-year-old epileptic patient underwent right hemicolectomy and cholecystectomy surgery under general endotracheal anesthesia. Anesthesia was maintained with sevoflurane, and sufentanil, rocuronium, and dexmedetomidine infusions. After the operation and confirmation of neuromuscular recovery, the patient woke from anesthesia within 15 min and successfully extubated. After the vital signs of patient were stable, the patient was transported to post anesthesia care unit (PACU). 6 h after the surgery, he fell into a stuporous state for lasting 14 h and EEG showed no epileptiform discharges. Stupor did re-occur in 2 days after operation. 36 hours after operation, all signs of the stuporous state resolved spontaneously. Apparent dexmedetomidine-induced stuporous state has not been reported in the human literature.

Keywords: Dexmedetomidine, stupor, epilepsy, abdominal surgery

Introduction

As part of a balanced anesthetic, a highly selective α_2 agonist dexmedetomidine has sedative and anxiolytic effects without respiratory depression [1-3], and provides neuroprotective and anticonvulsant properties [4]. It is reported that dexmedetomidine infusion is useful in epileptic patient undergoing surgery [5]. Dexmedetomidine is known to have several side effects, e.g. polyuric syndrome [6, 7]; however, apparent dexmedetomidine-induced stuporous state has not been reported in the human literature.

Case presentation

The patient was a 56-year-old man with a medical history notable for epilepsy, in Tongji Hospital. She complained of right abdominal pain for 3 days. 6 years ago, he was alive but couldn't wake up, and was admitted to our hospital with sudden loss of consciousness (stuporous state) without a prominent predisposing factor, including high fever or encephalitis, and he had not a personal or family history of neurologic disease, including epilepsy. Detailed examinations including hematological tests, electroencephalography (EEG), brain topography and brain computed tomography (CT) revealed no abnormalities, and he woke from stuporous state within 4 hours. 5 years ago, he had very small foam at the mouth, facial seizure, and limb ictal catatonia; these manifestations lasted for 1.5 min. He was admitted to our internal medicine ward, and epileptic seizure was diagnosed by EEG data showing obvious epileptiform discharges, and resolved with the administration of antiepileptic drugs (lamotrigine 100 mg, and magnesium valproate sustained release tablet 250 mg).

After obtaining written consent, he continued to take antiepileptic drugs and underwent right hemicolectomy and cholecystectomy surgery under general endotracheal anesthesia. Anesthesia was induced with propofol, sufentanil, and CIS-Atracurium, and maintained with the appropriate propofol, remifentanil, and dexmedetomidine (45 μg) infusions accompanied with an end-tidal CO_2 pressure ($PaCO_2$) between 35-45 mmHg [8-16]. After the operation and confirmation of neuromuscular recovery, the patient woke from anesthesia within 15 min and successfully extubated. After the vital signs of patient were stable, the patient was trans-

Figure 1. Photo of the patient 8 h after the onset of stupor. The patient fell into sudden loss of consciousness, without vomiting, foam at the mouth, limb seizure, and ictal catatonia.

ported to post anesthesia care unit (PACU). Surgery lasted 4.5 hours, and the blood loss was about 100 mL with a urine output of 1,300 mL.

6 h after the surgery, he suddenly fell into deep state of unconsciousness without vomiting, foam at the mouth, limb seizure, and ictal catatonia (**Figure 1**); Medical examination revealed coma state, no spoken language, no abnormal pathologic syndromes. He was alive but couldn't wake up, and unable to move or respond to his environment. EEG showed no epileptiform discharges (**Figure 2**). Arterial blood gas analysis (ABG) showed: pH 7.34, PCO_2 44.2 mmHg, Hb 13.7 g/dL, Hct 42%, Ca^{2+} 1.12 mmol/L, HCO_3 23.1 mmol/L, BE-2.2 (**Table 1**). Detailed examinations including complete blood chemistry tests, cervical vascular MRI and brain CT revealed no abnormalities except elevation of heart rate (122 bpm), blood alanine and aspartate aminotransferase (53 U/L and 41 U/L, respectively) and blood glucose (11.29 mmol/L). These manifestations were diagnosed to be stuporous state and lasted for 14 h. 20 h after the surgery, he regained consciousness with clear doctor-patient talk, and however, he had obvious retrograde amnesia.

Stupor did re-occur for lasting 4 h in 2 days after operation. 36 hours after operation, all signs of the stuporous state resolved spontaneously. On postoperative day 15, the patient was discharged from our hospital.

Discussion

Consciousness (Latin conscientia "moral conscience") is known to be defined as a continuous state of full awareness of the Self and one's relationship to the external and internal environment, describing the degree of wakefulness in which an organism recognizes stimuli in modern science [17-24]. Stuporous state is a deep state of unconsciousness, without vomiting, foam at the mouth, limb seizure, and ictal catatonia [25-27]. We studied the epileptic case of a 56-year-old man who lost consciousness after abdominal surgery, and hypothesized that dexmedetomidine might be considered to be a potential cause of stuporous state in epileptic patient.

Recent evidences have indicated that α_2-adrenergic receptor agonist dexmedetomidine plays an important role in sedation and sympatholysis [28-30]. It is important to note that dexmedetomidine activates α_2-adrenergic receptor to reduce the release of synaptic norepinephrine by negative feedback [29]. Some reports showed that the increase of noradrenaline levels in humans, dogs and mice are effective in alleviating cataplexy [31-34]. Study of Burgess et al. indicated that the activation of noradrenergic neurons in locus coeruleus (LC) resulted in the facilitation of activity of motor neurons, which in turn contributes to reduce muscle tone [32]. Our previous founding [35] suggested that injections of PRV-614 into the kidney resulted in retrograde infection of neurons in LC of the pontine [14, 36-46], and pseudorabies virus (PRV)-614-infecting cells were most heavily concentrated in LC (**Figure 3A**, **3D**), indicating that there exists a direct neuroanatomical pathway between the kidney and LC. Otherwise, fluorescence immunohistochemistry revealed that PRV-614/MC4R-GFP, PRV-614/tyrosine hydroxylase (TH), PRV-614/tryptophan hydroxylase (TPH) dual-labeled neurons were detected in LC (**Figure 3**), indicating that neuron in the LC is melanocortinergic, catecholaminergic and serotonergic. These data indicate that α_2-adrenergic receptor agonist dexmedetomidine may promote the stupor attack as acting on α_2-adrenergic receptor of noradrenergic neurons in the LC.

In summary, it is widely perceived that some patients with nonconvulsive epilepsy are known to exhibit stuporous state. We reported one case with apparent dexmedetomidine-induced stuporous state in epileptic patient undergoing abdominal surgery. Further investigation into the true incidence of stuporous state in epilep-

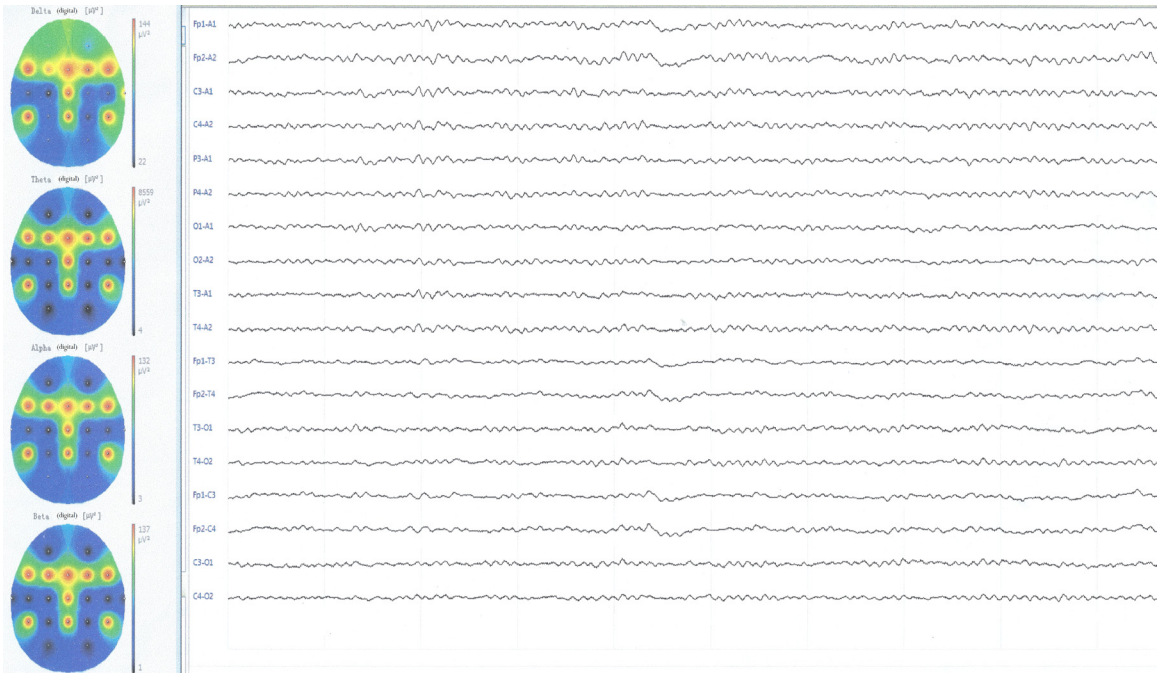

Figure 2. Electroencephalographic recording 2 h after the onset of stupor showed low amplitude in the left temporal region with loss of consciousness. EEG showed no epileptiform discharges.

Table 1. Arterial blood gas at different times

	pH	PCO_2	Hb	Hct	Na^+	K^+	Ca^{2+}	HCO_3	BE	Glu
Before operation	7.357	39.7	12.4	38	142.6	4.43	2.09	24.1	-2.1	7.23
During operation	7.351	42.3	13.6	40	142	4.0	1.28	24.8	0.3	6.54
3 h after operation	7.32	45.8	13.7	42	146	4.36	1.16	23.1	-2.6	11.19
6 h after operation	7.34	44.2	13.7	42	144	4.39	1.12	23.1	-2.2	11.29
2 d after operation	7.43	41.3	13.1	40	146	3.81	1.16	26.7	2.6	9.12
6 d after operation	7.36	40.1	10.9	30.8	142	3.86	2.01	29.2	2.7	6.58
11 d after operation	7.38	39.3	10.1	30.1	140.3	4.93	2.23	23.9	1.0	6.46

tic patient after dexmedetomidine injection is warranted.

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Disclosure of conflict of interest

None.

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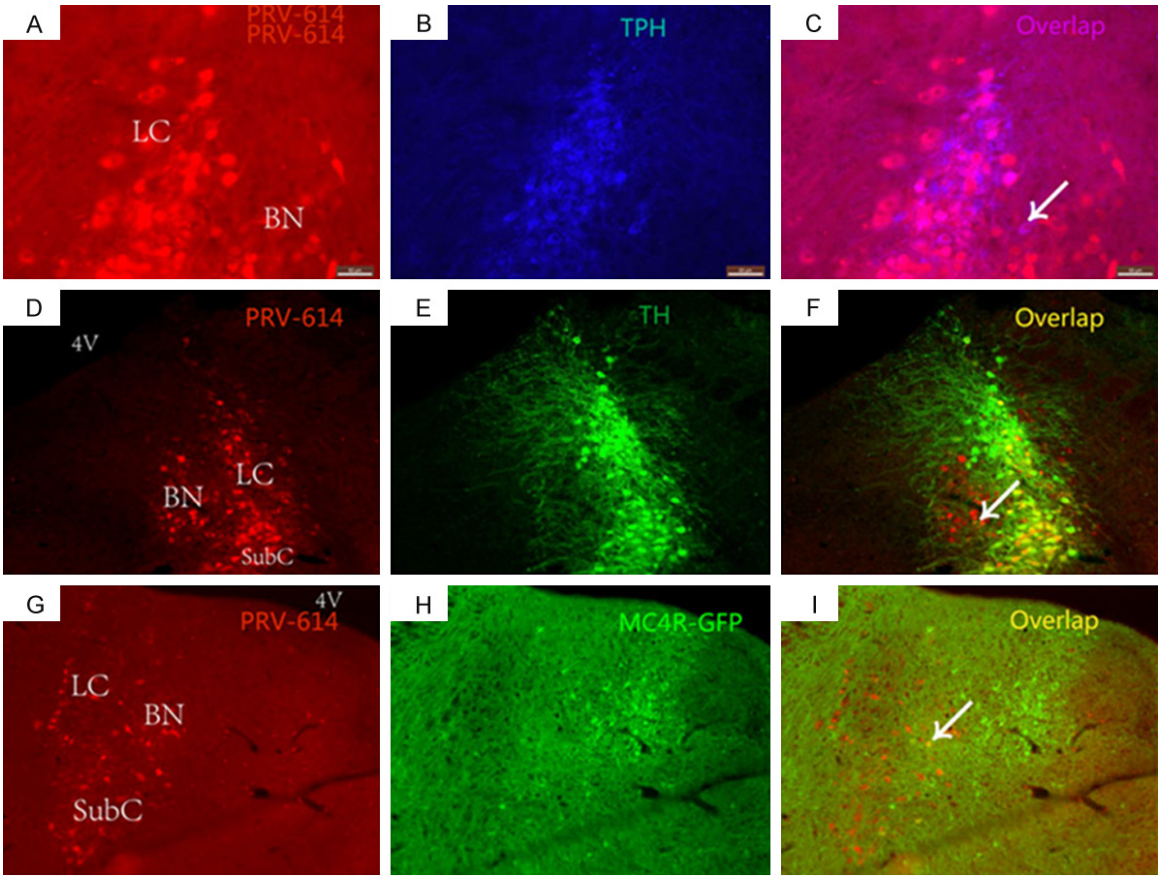

Figure 3. Colocalization of TPH (blue) and TH (green) in subsets of PRV-614-positive neurons (red) within LC areas. (A, D, G) PRV-614-expressing neurons; (B) TPH-expressing neurons in the same section as (A); (E) TH-expressing neurons in the same section as (D); (H) MC4R-GFP-expressing neurons in the same section as (G); (C) Overlap of (A) and (B), depicting distribution of TPH-IR and PRV-614-bearing neurons; (F) Overlap of (D) and (E), depicting distribution of TH-IR and PRV-614-bearing neurons; (I) Overlap of (G) and (H), depicting distribution of MC4R-GFP-expressing and PRV-614-bearing neurons; Scale bar: 50 μm for (A-C), 25 μm for (D-F) and (G-I), 4V, Fourth ventricle; BN, Barrington's nucleus; LC, locus coeruleus; SubC, locus subcoeruleus; TH, tyrosine hydroxylase; TPH, tryptophan hydroxylase. Some drawings were taken from HB Xiang (*Acta Neurochirurgica*, 2013).

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