 doi: 10.2176/jns-nmc.2022-0333

*NMC Case Report Journal 10, 197-202, 2023*

# *Nonconvulsive Status Epilepticus Associated with Cerebral Hyperperfusion Syndrome after Carotid Endarterectomy: A Case Report*

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## Abstract

**We report a case of a 73-year-old man who developed nonconvulsive status epilepticus as a complication of cerebral hyperperfusion syndrome after carotid endarterectomy for carotid artery stenosis. On postoperative day 1, the patient experienced headaches and vomiting. Resting *N*-isopropyl-*p*-[$^{123}$I] iodoamphetamine single-photon emission computed tomography showed increased cerebral blood flow to the entire right hemisphere, and the patient was diagnosed with cerebral hyperperfusion syndrome. He was treated with antihypertensive and antiseizure medications, sedated using propofol, intubated, and placed under mechanical ventilation. On postoperative day 3, computed tomography perfusion imaging showed a reduction in hyperperfusion, and propofol sedation was terminated on postoperative day 4. However, the patient exhibited prolonged impaired awareness and roving eye movements, and long-term video electroencephalographic monitoring revealed electrographic seizures. The patient was diagnosed with nonconvulsive status epilepticus. Propofol sedation was resumed, and the antiseizure medication dose was increased. Subsequently, the state of hyperperfusion in the right hemisphere diminished, and electroencephalographic findings improved, allowing sedation to be terminated on postoperative day 7. The findings from this case suggest that when clinical subtle symptoms, such as impaired awareness and roving eye movements, are observed during treatment of cerebral hyperperfusion syndrome, video electroencephalography should be performed to detect electrographic seizures.**

Keywords: nonconvulsive status epilepticus, cerebral hyperperfusion syndrome, carotid endarterectomy, epileptiform discharges, long-term video electroencephalographic

## Introduction

Cerebral hyperperfusion syndrome (CHS) following carotid endarterectomy (CEA) is caused by cerebrovascular autoregulation failure and has a reported incidence of <3%. Symptoms include headache, pain in the face or eyes, vomiting, an altered level of consciousness, visual field defects, seizures, and focal neurological symptoms.[1] Severe intracerebral hemorrhage occurs in approximately 1% of patients with carotid artery stenosis who had undergone CEA or carotid artery stenting, with a mortality rate of 26%.[2] Although seizures are a major indicator of CHS, few studies have focused on the relationship between seizures and CHS.[3]

Nonconvulsive status epilepticus (NCSE) was first reported by Gastaut in 1963, in which patients experienced prolonged seizures without motor symptoms.[4] NCSE has received attention as the cause of unexplained disorders of consciousness among intensive care patients and has a reported mortality rate of 52%.[5] According to recent reports, 8.8% of patients with acute cerebral hemorrhage and 15% of patients with subarachnoid hemorrhage following surgery develop NCSE.[6,7] Cases of NCSE associated with CHS following superficial temporal artery-to-middle cerebral ar-

Received October 22, 2022; Accepted April 10, 2023

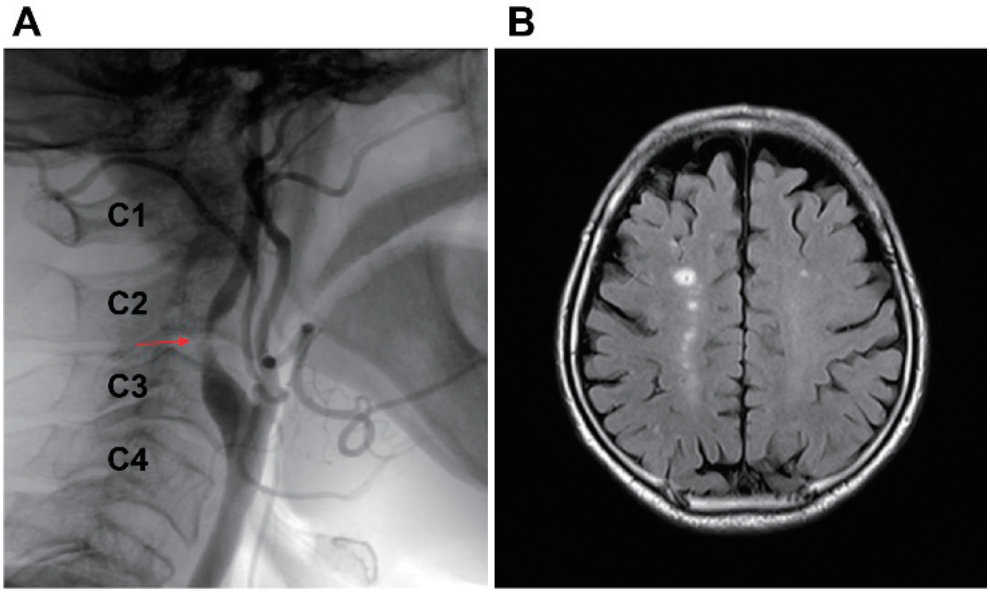


**Fig. 1 Preoperative images. (A) Angiography showing stenosis (arrow in red) of the cervical portion of the right internal carotid artery from the superior margin of the C3 vertebral body to the midline of the C2 vertebral body. Stenosis is 80% according to the North American Symptomatic Carotid Endarterectomy Trial criteria. (B) Preoperative cerebral fluid-attenuated inversion recovery magnetic resonance imaging showing an old cerebral watershed infarction of the right frontal centrum semiovale. The red arrow indicates the point of stenosis.**

tery (STA-MCA) bypass or CEA were also reported.[8-10)]

We report a case of NCSE associated with CHS following CEA, in which we detected electrographic seizures (ESz) with subtle clinical signs using long-term video electroencephalography (VEEG).

## Case Report

The patient was a 73-year-old man with a 20-year history of smoking 20 cigarettes/day. He had a history of stroke, hypertension, dyslipidemia, diabetes, chronic kidney disease, and myocardial infarction (for which he underwent stent treatment approximately 30 years ago), but he had no history of epilepsy. The patient was referred to our facility for the surgical treatment of symptomatic right internal carotid artery (ICA) stenosis. Six months earlier, he experienced left upper limb paresis and was treated for a right frontal lobe watershed infarction in another hospital. The patient was taking aspirin and clopidogrel as prescribed by his previous doctor. During his outpatient course, he experienced transient left upper and lower limb paresis due to a transient ischemic attack (TIA) following mild dehydration.

Preoperative examination revealed high-grade stenosis of the left main coronary artery and a low ejection fraction of approximately 40%, indicating poor cardiac function. Blood tests showed an estimated glomerular filtration rate of 40.0 mL/min/1.73 $m^2$, a low-density lipoprotein cholesterol level of 62.1 mg/dL, and a glycated hemoglobin level of 5.7%. Cerebral angiography showed 80% right ICA stenosis from the superior margin of the C3 vertebral body to the midline of the C2 vertebral body (Fig. 1A). The degree of ICA stenosis was measured using the North American Symptomatic Carotid Endarterectomy Trial method. Hypoplasia of the operative side of the anterior cerebral artery (A1) and the posterior communicating artery was observed. Cerebral magnetic resonance imaging (MRI) fluid-attenuated inversion recovery (FLAIR) imaging revealed an old cerebral watershed infarction of the right frontal centrum semiovale (Fig. 1B). Intracranial and cervical magnetic resonance angiography (MRA) rendering, particularly on the operative side of the MCA from M2 and beyond, was poor and showed decreased signal intensity. MRI plaque imaging showed high intensity on T1- and T2-weighted imaging and magnetization prepared rapid acquisition with gradient echo, suggesting the presence of unstable plaques. Resting *N*-isopropyl-*p*-[$^{123}$I] iodoamphetamine single-photon emission computed tomography ($^{123}$I-IMP SPECT) showed a widespread reduction in cerebral blood flow (CBF) to the right hemisphere (Fig. 2A). Therefore, this patient was considered at a high risk of postoperative CHS. Considering the results of the preoperative examination and the patient's history of cerebral infarction, we chose to address the right ICA stenosis through surgical intervention. Aspirin was administered once before the surgery. We scheduled CEA to address the right ICA stenosis. Three weeks before CEA, a coronary bypass for severe coronary artery stenosis was performed in our facility. We performed CEA with shunting while monitoring the somatosensory evoked potential (SEP), motor evoked potential

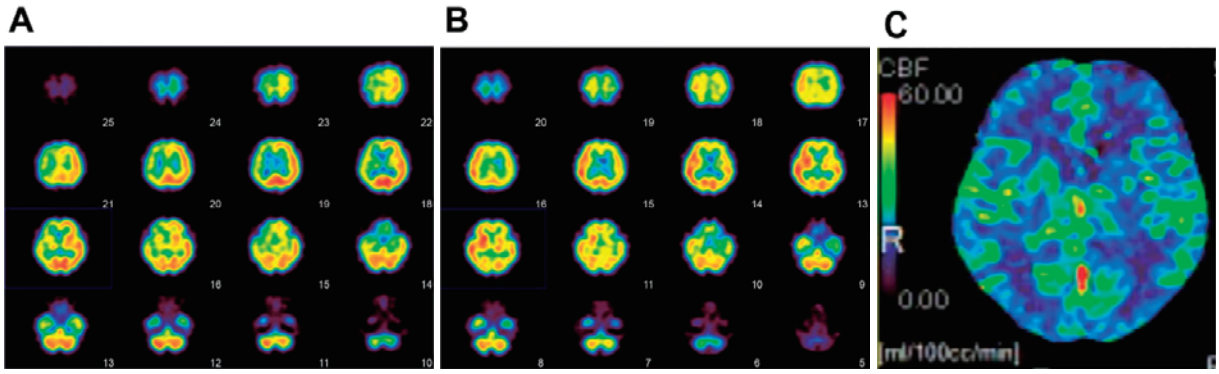


**Fig. 2** ***N*-Isopropyl-*p*-[$^{123}$I] iodoamphetamine single-photon emission computed tomography ($^{123}$I-IMP SPECT). (A) Preoperative $^{123}$I-IMP SPECT showing widespread reduction in the cerebral blood flow (CBF) (blue) in the right hemisphere. (B) Emergency $^{123}$I-IMP SPECT performed on postoperative day 1 showing widespread CBF elevation (red) in the right hemisphere. (C) CT perfusion performed on postoperative day 3 showing no CBF laterality.**

(MEP), and regional cerebral oxygen saturation ($rSO_2$) (INVOS5100; Somanetics Corporation, Troy, MI, USA). The procedure was completed with no notable drops in the SEP or MEP.

After surgery, the patient was alert and the neurological findings were normal. Considering the possibility of CHS developing immediately after surgery, the patient's systolic blood pressure was maintained at ≤120 mmHg, and the $rSO_2$ was continuously monitored. MRI on postoperative day 1 revealed no evidence of cerebral infarction or hemorrhage. Around noon on the same day, the patient began to experience generalized headache and vomiting, with a blood pressure of 144/68 mmHg. Emergency $^{123}$I-IMP SPECT confirmed elevated CBF on the operative side, and the ratio of CBF in the unaffected to the affected side was more than two times greater than that before surgery (Fig. 2B). On the day of the operation, the $rSO_2$ remained approximately 60%, with almost no laterality. However, when symptoms developed on postoperative day 1, the operative side (right) $rSO_2$ was 67% and the nonoperative side (left) $rSO_2$ was 57%, showing an increase of approximately 10% on the operative side. We were unable to identify the cause, such as cerebral infarction, of the headache and vomiting using MRI. Thus, the patient was diagnosed with CHS on the basis of the test results.

For the treatment of CHS, we initiated sedation under propofol with ventilator management as well as lacosamide (LCM; 100 mg/day), a novel antiseizure medication (ASM). CT perfusion performed on postoperative day 3 showed no CBF laterality (Fig. 2C), and sedation was terminated on postoperative day 4. However, 1 day after discontinuing sedation with propofol, the patient showed prolonged impaired awareness and roving eye movements. Therefore, we suspected NCSE and performed 6-h VEEG monitoring. The 6-h VEEG showed generalized periodic discharges averaging 1.6 Hz (Fig. 3A) transferred to epileptiform discharges averaging >2.5 Hz for at least 10 s (Fig. 3B), which met the criteria of ESz according to the American Clinical Neurophysiology Society's (ACNS) standardized critical-care electroencephalography (EEG) terminology (2021 version). The patient was diagnosed with NCSE. We administered intravenous diazepam. Additionally, we resumed sedation with propofol and increased the dose of LCM to 200 mg/day. EEG on postoperative day 7 showed improvement in EEG findings (Fig. 4). Thus, sedation was terminated, and the patient was extubated. $^{123}$I-IMP SPECT on postoperative day 9 showed that the CBF imbalance between the two hemispheres had abated.

After the NCSE resolved, the patient presented with focal impaired awareness seizure, and the final ASM required an additional dose of levetiracetam 2000 mg/day. FLAIR MRI on postoperative day 90 showed no new structural lesions (Fig. 5). The patient underwent comprehensive rehabilitation and was discharged to his home with a modified Rankin scale score of 2 on postoperative day 96. The patient consented to the publication of this report.

## Discussion

We herein reported a case of NCSE associated with CHS after CEA. Seizures following CEA have been reported to occur at a frequency of 0.5%,[11] and a case of focal motor status epilepticus as the only symptom of CHS after CEA was recently reported.[12] De Liso et al.[9] reported a case of NCSE associated with CHS following CEA, but they did not present EEG findings. Hamamura et al.[8] reported a case of NCSE associated with CHS following STA-MCA bypass for MCA occlusion. In their report, the patient was diagnosed with NCSE after exhibiting impaired awareness and worsening paresis after surgery, as well as rhythmic delta waves with EEG evolution.

Reduced cerebrovascular reserve capacity, postoperative hypertension, and prolonged postoperative hyperperfusion are known risk factors for CHS after CEA.[1] CHS requires appropriate treatment early on to prevent complications such as severe cerebral edema or cerebral hemorrhage,

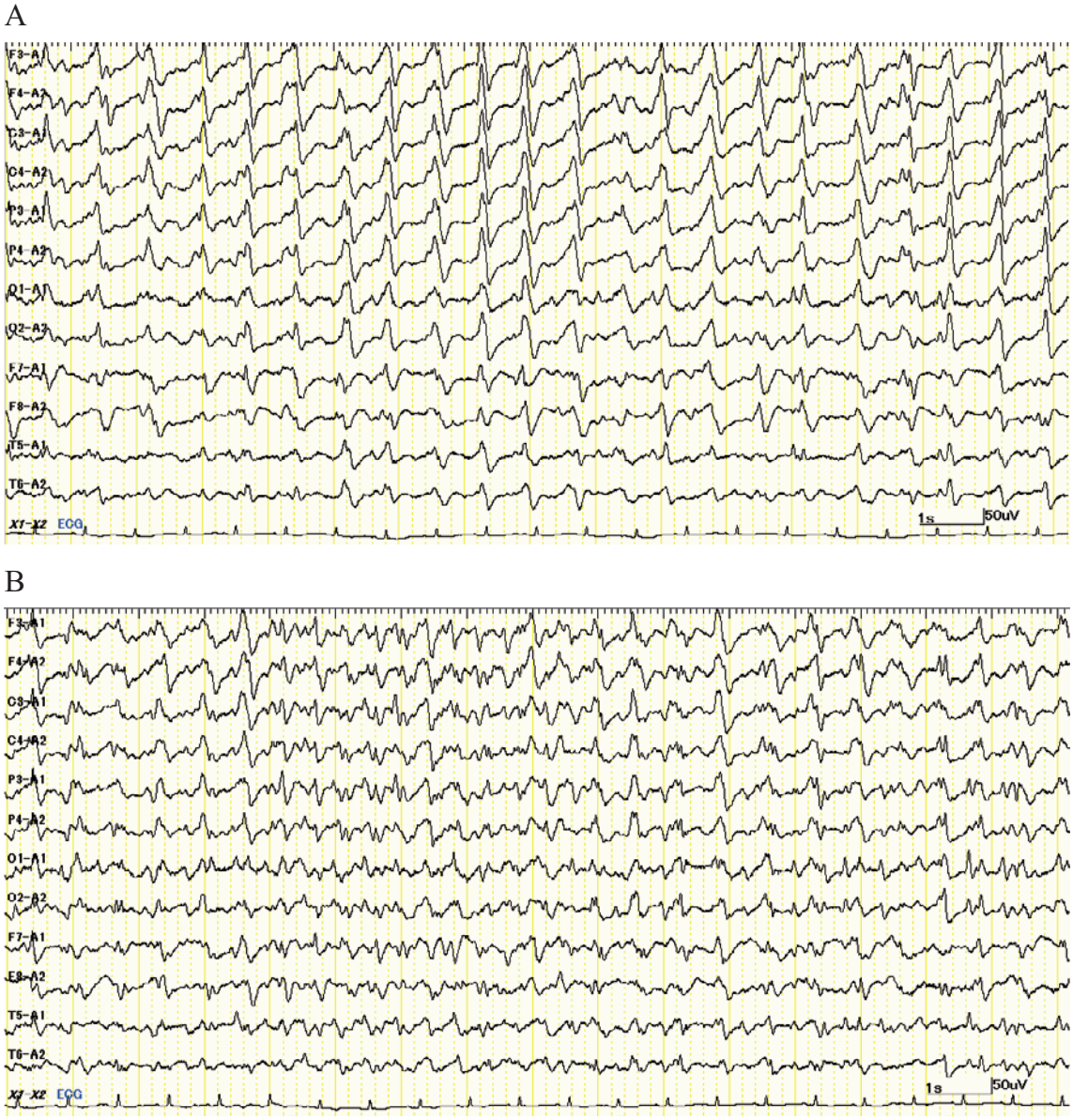


**Fig. 3 Long-term video electroencephalographic monitoring performed on postoperative day 4 showing generalized periodic discharges averaging 1.6 Hz (A) transferred to epileptiform discharges averaging >2.5 Hz (B) for at least 10 s. The patient exhibited prolonged impaired awareness and roving eye movements.**

and antihypertensive treatment is essential in controlling cerebral perfusion pressure.[1,2] Acetazolamide challenge $^{123}$I-IMP SPECT was not performed in the current case because the patient's coronary artery disease meant that he was at a high risk of developing severe side effects. We further considered the patient at a high risk of CHS before surgery as he exhibited TIA due to mild dehydration before the operation, his preoperative resting SPECT showed decreased CBF in the right hemisphere compared with the left hemisphere, and MRA rendering from the right M2 and beyond was poor. In accordance with a report by Ogasawara et al.,[11] we administered edaravone before the perioperative clamping of the ICA to prevent CHS. Despite this measure and ensuring that the postoperative blood pressure remained strictly at ≤120 mmHg, the patient developed CHS. We administered treatment with intubation, mechanical ventilation, and sedation using propofol.

The ACNS's standardized critical-care EEG terminology (2021 version)[13] defined nonconvulsive seizures (NCS) as ESz, which were either epileptiform discharges averaging >2.5 Hz for ≥10 s or any electrographic pattern with definite evolution lasting ≥10 s. The latter has evolution of frequency, morphology, or location. NCSE was defined as electrographic status epilepticus: ESz for ≥10 continuous minutes or for a total duration of ≥20% of any 60-min period of recording. In this case, EEG findings showed 1.6-Hz

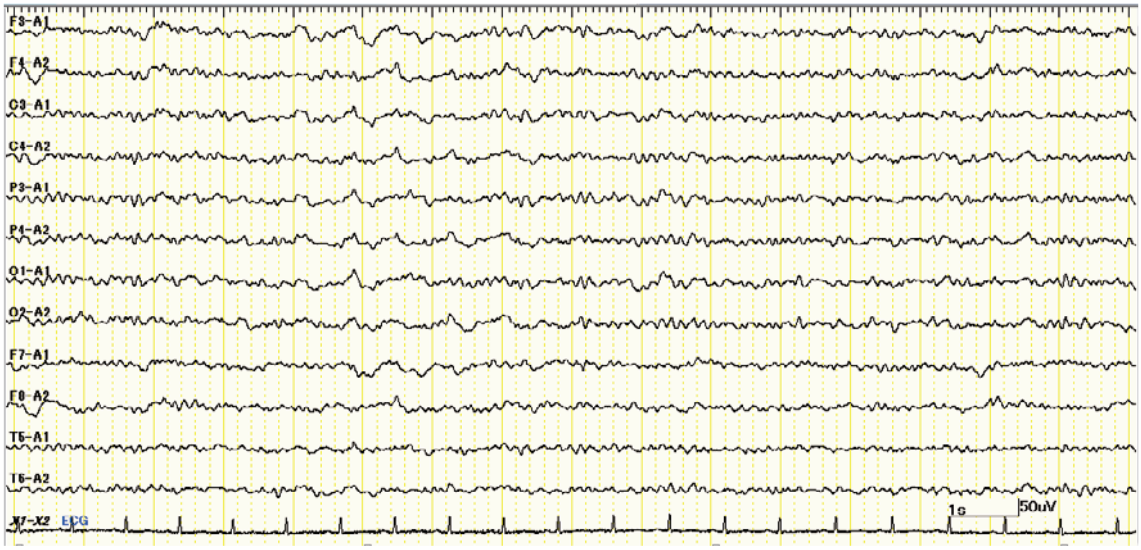


**Fig. 4 Interictal electroencephalographic monitoring on postoperative day 7 showing improvement in epileptic discharges.**

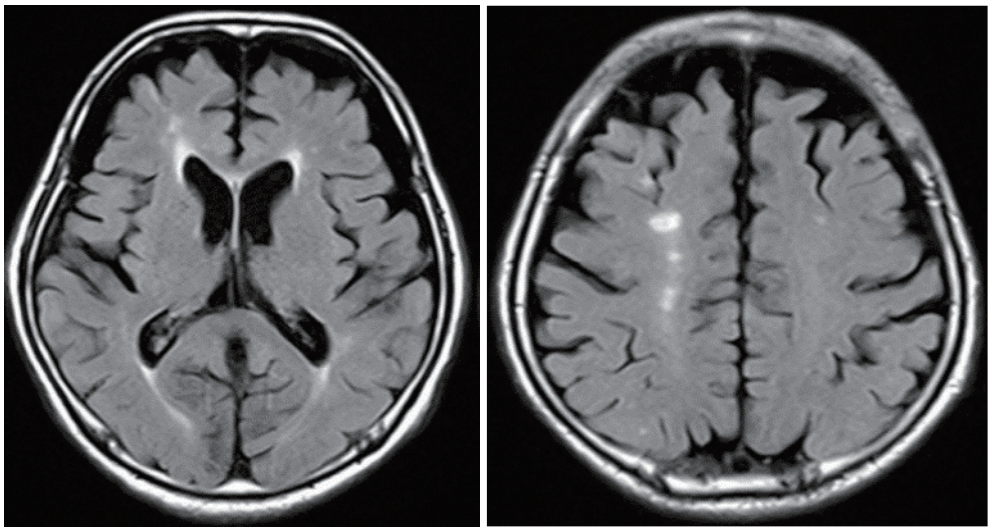

**Fig. 5 Postoperative cerebral fluid-attenuated inversion recovery magnetic resonance imaging on postoperative day 90 showing no new structural lesions.**

generalized periodic discharges transferred to epileptiform discharges >2.5 Hz for at least 10 s. As we used diazepam and resumed sedation immediately, we were unable to confirm if the seizure would last for more than 10 min. We diagnosed NCSE with coma clinically. The ACNS also defined electroclinical seizure, which is either definite clinical correlate time-locked to the pattern or EEG and clinical improvement with a parenteral (typically intravenous) ASM.[13] NCSE can be associated with clinical subtle signs, such as altered mental status, speech disturbance, face and limb myoclonus, nystagmus, eye subtle movement, eye deviation, pupillary abnormalities, and automatic instability.[14,15] In EEG diagnosis, especially of NCSE, the ACNS defined ESz clearly.[13] Recently, with widespread use and improved understanding of critical-care EEG, reports of NCSE have been gradually increasing.[6-10] There is a possibility that NCSE associated with CHS is more frequent than expected, regardless of post-CEA status. In an intensive care unit setting with continuous EEG, 90% of NCS or NCSE can be detected in the first 24-48 h.[16] If continuous EEG is not available, 30-min EEG can also be used to detect most epileptiform abnormalities.[17]

A limitation of this report is that we did not perform continuous EEG (cEEG) monitoring immediately after CHS diagnosis. Hence, we may have missed any abnormal signs of NCSE, thereby delaying the diagnosis. Additionally, the cEEG monitoring that we performed was limited to 6 h. Therefore, we did not confirm the real-time improvement of its findings following the administration of ASMs through simultaneous cEEG recording.

In conclusion, the present case suggests that when we observe clinical subtle symptoms such as impaired awareness and roving eye movements during CHS treatment, we believe that VEEG should be performed as soon as possible to detect ESz.

## Acknowledgments

We would like to thank Editage (www.editage.com) for English language editing.

## Conflicts of Interest Disclosure

The authors have no conflict of interest. Authors who are members of the Japan Neurosurgical Society have registered their online self-reported conflict of interest disclosure statement forms.

## References

1) van Mook WN, Rennenberg RJ, Schurink GW, et al.: Cerebral hyperperfusion syndrome. *Lancet Neurol* 4: 877-888, 2005
2) Ogasawara K, Sakai N, Kuroiwa T, et al.: Intracranial hemorrhage associated with cerebral hyperperfusion syndrome following carotid endarterectomy and carotid artery stenting: retrospective review of 4494 patients. *J Neurosurg* 107: 1130-1136, 2007
3) MacGillivray DC, Valentine RJ, Rob CG: Reperfusion seizures after innominate endarterectomy. *J Vasc Surg* 6: 521-523, 1987
4) Gastaut H: Clinical and electroencephalographical classification of epileptic seizures. *Epilepsia* 11: 102-113, 1970
5) Litt B, Wityk RJ, Hertz SH, et al.: Nonconvulsive status epilepticus in the critically ill elderly. *Epilepsia* 39: 1194-1202, 1998
6) Kikuta Y, Kubota Y, Nakamoto H, Chernov M, Kawamata T: Nonconvulsive status epilepticus after surgery for ruptured intracranial aneurysms: incidence, associated factors, and impact on the outcome. *Clin Neurol Neurosurg* 200: 106298, 2021
7) Tomori S, Tanaka T, Matsubara S, et al.: Risk factors for nonconvulsive status epilepticus after stroke. *Eur Neurol* 80: 256-260, 2018
8) Hamamura T, Morioka T, Sayama T, et al.: Cerebral hyperperfusion syndrome associated with non-convulsive status epilepticus following superficial temporal artery-middle cerebral artery anastomosis. Case report. *Neurol Med Chir (Tokyo)* 50: 1099-1104, 2010
9) De Liso A, Ricci L, Bravi MC, Pezzella FR, Anticoli S: An uncommon case of nonconvulsive status epilepticus successfully treated with enteral Brivaracetam. *Acta Biomed* 92: e2021156, 2021
10) Morioka T, Sayama T, Shimogawa T, et al.: Electroencephalographic evaluation of cerebral hyperperfusion syndrome following superficial temporal artery-middle cerebral artery anastomosis. *Neurol Med Chir* 53: 388-395, 2013
11) Ogasawara K, Inoue T, Kobayashi M, et al.: Pretreatment with the free radical scavenger edaravone prevents cerebral hyperperfusion after carotid endarterectomy. *Neurosurgery* 55: 1060-1067, 2004
12) Edwards AM, Birchler CR, Park S, Baker JM, Molnar RG: Cerebral hyperperfusion syndrome presenting as status epilepticus following carotid endarterectomy. *Cureus* 13: e20551, 2021
13) Hirsch LJ, Fong MWK, Leitinger M, et al.: American Clinical Neurophysiology Society's standardized critical care EEG terminology: 2021 version. *J Clin Neurophysiol* 38: 1-29, 2021
14) Friedman D, Claassen J, Hirsch LJ: Continuous electroencephalogram monitoring in the intensive care unit. *Anesth Analg* 109: 506-523, 2009
15) Classen J, Mayer SA, Kowalski RG, Emerson RG, Hirsch LJ: Detection of electrographic seizures with continuous EEG monitoring in critically ill patients. *Neurology* 62: 1743-1748, 2004
16) Sutter R, Semmlack S, Kaplan PW: Nonconvulsive status epilepticus in adults insights into the invisible. *Nat Rev Neurol* 12: 281-293, 2016
17) Abend NS, Dlugos DJ, Hahn CD, Hirsch LJ, Herman ST: Use of EEG monitoring and management of non-convulsive seizures in critically ill patients: a survey of neurologists. *Neurocrit Care* 12: 382-389, 2010

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