



Case Report

Verbal and memory deficits caused by aphasic status epilepticus after resection of a left temporal lobe glioma

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ABSTRACT

Background: Nonconvulsive status epilepticus (NCSE) is induced by common neurosurgical conditions, for example, trauma, stroke, tumors, and surgical interventions in the brain. The aggressiveness of the treatment for NCSE depends on its neurological prognosis. Aphasic status epilepticus (ASE) is a subtype of focal NCSE without consciousness impairment. The impact of ASE on neurological prognosis is poorly documented. We describe a case of postoperative ASE resulting in verbal and memory deficits.

Case Description: A 54-year-old, right-handed man with focal impaired awareness seizures underwent partial resection for a left temporal lobe tumor. No neurological deficits were observed immediately after surgery. Three days later, however, a focal to bilateral tonic-clonic seizure (FBTCS) occurred, followed by aphasia. Electroencephalography revealed 1.5 Hz left-sided periodic discharges. He was diagnosed with ASE. Multiple anti-seizure drugs were ineffective for the resolution of the patient's verbal disturbance. Nine days after the FBTCS, deep sedation with intravenous anesthetics was performed and the ASE stopped. Thereafter, his symptoms gradually improved. However, the prolonged ASE resulted in verbal and memory deficits. Automated hippocampal volumetry revealed an approximate decrease of 20% on the diseased side on magnetic resonance imaging 3 months after surgery.

Conclusion: Prolonged ASE can induce verbal and memory deficits. Early intervention with intravenous anesthetics is required to obtain a favorable neurological prognosis.

Keywords: Aphasic status epilepticus, Intravenous anesthetics, Memory disturbance, Nonconvulsive status epilepticus, Verbal deficit

INTRODUCTION

Nonconvulsive status epilepticus (NCSE) has been attracting increasing attention in neurosurgical practice after the Salzburg criteria were published.^[11] It can be induced by common neurosurgical conditions, for example, trauma, stroke, tumors, and surgical interventions in the brain. In spite of the variety of therapeutic options, the optimal treatment for NCSE and its subtypes remains to be established. Since treatment guidelines are scant, NCSE with coma and focal NCSE with consciousness impairment are mainly treated with intravenous anesthetics when these conditions are uncontrollable.^[14] However, there is little evidence to determine whether focal NCSE without consciousness impairment should be aggressively treated with

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intravenous anesthetics. In addition, the optimal timeline for such aggressive intervention remains unclear. Knowledge of the effects of patients' epilepsy on their neurological prognosis allows for the determination of treatment intensity. However, such effects of focal NCSE without impairment of consciousness are poorly documented. Here, we describe a case of aphasic status epilepticus (ASE), a subtype of focal NCSE without consciousness impairment, which occurred after resection of a glioma in the left temporal lobe. Despite the combined use of multiple anti-seizure drugs (ASDs), the patient experienced verbal and memory sequelae. Intravenous anesthetics were effective in controlling the epileptic activities in this case; however, early intervention is required for a favorable neurological prognosis in ASE.

CASE DESCRIPTION

A 54-year-old, right-handed man had experienced two episodes of focal impaired awareness seizures and was taking levetiracetam. Magnetic resonance imaging (MRI) revealed a high-intensity lesion of the temporal lobe on fluid-attenuated inversion recovery-weighted images, and a noncontrast-enhanced cyst appeared inside the temporal lobe at the 1-year follow-up, suggesting the presence of a low-grade brain tumor [Figure 1a and b]. The patient was referred to our hospital for treatment. He spoke fluently and had an average memory as determined with the revised Wechsler memory scale (WMS-R) [Table 1]. Long-term electroencephalographic (EEG) monitoring revealed interictal epileptiform discharges of the left temporal lobe, a rare finding. As a Wada test revealed that the left hemisphere was dominant in terms of language and memory, the medial temporal structures were reserved for functional preservation by performing a partial resection [Figure 1c]. Histopathological examination revealed diffuse astrocytic gliomas. Genomic analysis indicated that the *IDH* gene and the *TERT* promoter were wild type, and the *MGMT* promoter was unmethylated. Therefore, we diagnosed this tumor as a diffuse astrocytoma, *IDH*-wild type, according to the 2016 World Health Organization classification [Figure 1e and f].

No neurological deficits were observed immediately after surgery. However, 3 days later, a focal to bilateral tonic-clonic seizure (FBTCS) occurred, followed by aphasia. The verbal disturbance was initially presumed to be a part of the postictal state; however, these symptoms persisted even as his eating, walking, and comprehension returned to baseline levels. The presence of ischemic complications was excluded using diffusion-weighted MRI. This suggested that NCSE, such as ASE, could be responsible for the language disturbance. Therefore, levetiracetam was increased to the maximum dosage of 3000 mg/day, and lacosamide was additionally administered at 200 mg/day. However, their efficacy was limited. Four days after the FBTCS, EEG revealed 1.5 Hz

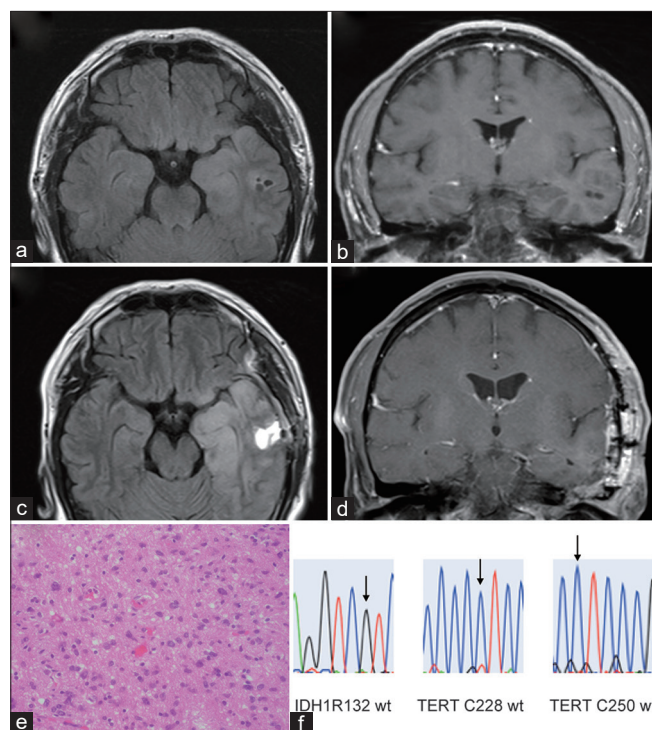


Figure 1: (a) Preoperative fluid-attenuated inversion recovery magnetic resonance imaging (FLAIR-MRI) revealing a high-intensity area with a cyst component in the left temporal lobe. (b) Preoperative contrast-enhanced T1-weighted (T1WCE) MRI revealing no enhancement. (c) Postoperative FLAIR-MRI indicating the partial removal of the tumor. (d) Postoperative T1WCE-MRI. Note that the inferior horn of the left lateral ventricle is enlarged. This may be explained by a reduction in the mass effect and hippocampal volume loss [Table 1]. (e) The hematoxylin-and-eosin-stained specimen is consistent with an astrocytic glioma. (f) Genomic analysis indicates that the *IDH* gene and *TERT* promoter are wild type.

left-sided periodic discharges (PDs) and ictal spatiotemporal evolution of rhythmic activity, which demonstrated that the ASE persisted [Figure 2]. The ineffectiveness of treatment with subsequent additional ASDs (fosphenytoin, perampanel, and clobazam) led us to choose aggressive treatment with intravenous anesthetics 9 days after the FBTCS. Forty-eight hours of deep sedation with induction of burst suppression terminated the NCSE pattern, and the patient's verbal disturbance gradually improved. Three days after administration of the intravenous anesthetics, an EEG revealed the disappearance of the PDs. However, verbal deficits remained at 3 weeks after surgery, predominantly in object naming and word retrieval, with a total score of 82 in the Western Aphasia Battery (WAB) [Table 1]. No improvement in the WAB score at the 3-month follow-up indicated that permanent complications had occurred.

In addition, a decrease in the indices of the WMS-R demonstrated substantial memory impairment after the

Table 1: Pre- and post-operative neuropsychological assessment and hippocampal volume.

	Preoperative	Postoperative	
		3 weeks	3 months
WMS-R			
Verbal memory	101		51
Visual memory	108		87
General memory	104		57
Attention/concentration	123		110
Delayed recall	107		68
WAB			
Oral expression quotient (20)		16	16
Auditory comprehension quotient (10)		9.4	8.8
Naming quotient (10)		5.6	4.0
Reading quotient (10)		10	7.8
Writing quotient (10)		10	8.6
Aphasia quotient (100)		82	75
Hippocampal volume (mm ³)			
Disease side	5447		4450
Unaffected side	4250		4060

WMS-R: Wechsler memory scale revised, WAB: Western aphasia battery

prolonged ASE. Automated hippocampal volumetry, conducted with the FreeSurfer software suite (<http://surfer.nmr.mgh.harvard.edu>), revealed an approximate decrease of 20% on the diseased side on MRI 3 months after surgery [Figure 1d]. Five months after the initial diagnosis, the patient died because of tumor progression.

DISCUSSION

We describe a case of ASE after surgery for a glioma in the left temporal lobe that resulted in verbal and memory sequelae. The clinical course of the patient demonstrates two important clinical issues. First, focal NCSE without consciousness impairment, such as ASE, can induce verbal and memory deficits. Second, intravenous anesthetics can halt ASE; however, early intervention is required for a favorable neurological prognosis.

ASE is a subtype of focal NCSE that is not accompanied by impaired consciousness, and it induces verbal disturbance during status epilepticus. While NCSE with coma or impaired awareness is notorious for poor neurological prognoses, verbal disturbance caused by ASE normally resolves, even if improvement is gradual.^[2,4,12] However, in a recent study, approximately 30% of patients with ASE developed mild-to-moderate aphasia, which is consistent with our case.^[1] Given that the etiology of ASE includes malignant brain tumors, stroke, and encephalitis, it is usually difficult to determine whether verbal disturbance is solely due to epileptic activities. However, our case demonstrated that ASE can induce verbal deficits, as there

were no obvious exacerbations other than the epileptic events.

The association between ASE and memory sequelae remains unclear. Complex partial status epilepticus (CPSE), another subtype of NCSE, can cause permanent cognitive and memory dysfunction.^[9] This suggests that epileptic activity in the temporal lobe can induce memory deficit. Consistent with our case, hippocampal atrophy following NCSE was previously suggested as a mechanism by which epileptic events exert a negative effect on memory function in CPSE.^[6,17] To the best of our knowledge, this is the first report to show that ASE induces memory deficits with hippocampal volume loss. Further clinical studies are necessary to verify this association.

In this study, intravenous anesthetics halted ASE that was refractory to multiple ASDs.^[10] They are one of the treatment options for focal NCSE; however, the optimal timeline for intervention has not yet been established.^[10] The time point at which a delay in treatment results in disability is a key factor in deciding the timing of intervention for status epilepticus. Convulsive status epilepticus lasting more than 30 min can induce neuronal damage. On the other hand, it remains unclear whether focal NCSE without impaired consciousness, including ASE, also has such a critical time point.^[16] Our case demonstrated that prolonged ASE can cause neurological sequelae, suggesting that there is indeed a critical period before which seizures have to be stopped in a patient with ASE. In support of this result, a previous study indicated that ASE lasting for 8 h can induce neurological

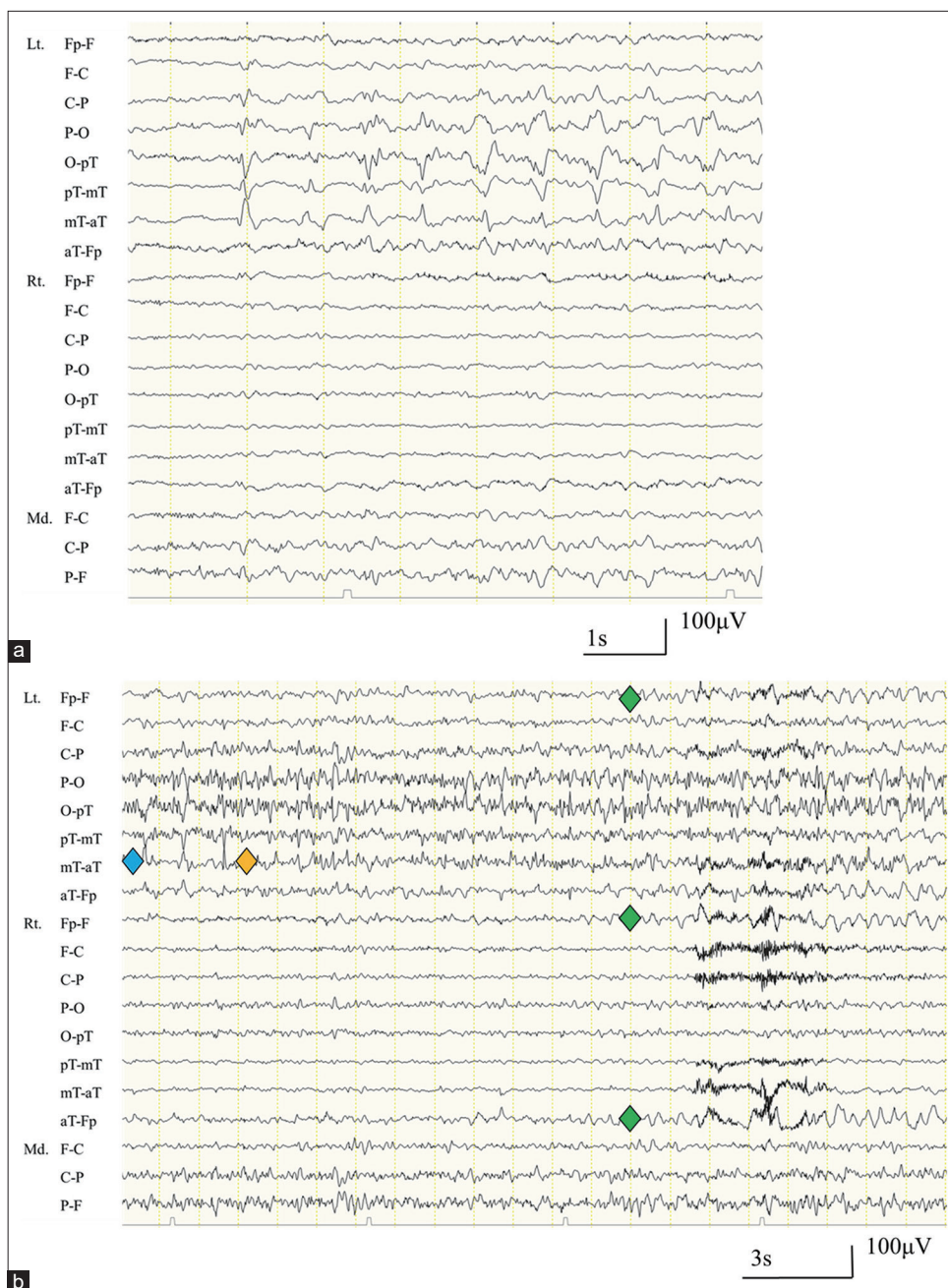


Figure 2: (a) An electroencephalograph (EEG; longitudinal bipolar montage), taken 4 days after the focal to bilateral tonic-clonic seizure, reveals 1.5 Hz periodic discharges with a maximum amplitude in the left temporal area. (b) An EEG revealing spatiotemporal evolution of epileptic discharges, indicating nonconvulsive status epilepticus (blue: periodic discharges, yellow: temporal evolution, green: spatial evolution). Lt: Left, Rt: Right, Fp: Front polar, F: Frontal, C: Central, P: Parietal, O: Occipital, pT: Posterior temporal, mT: Mid-temporal, aT: Anterior temporal, Md: Midline.

deficits.^[1] Therefore, the critical period before stopping ASE, which may be shorter than that previously assumed, should be identified. Other key determinants for ASE treatment include its etiology, the efficacy of nonaggressive treatment, and mortality due to aggressive treatment.^[5] However, it takes time to assess the efficacy of nonaggressive treatments. Therefore, if the etiology is a minor driver of the symptoms,

as in our case, early aggressive intervention, including the administration of intravenous anesthetics, may prevent neurological sequelae in patients with ASE.

Although early intervention is required for a favorable neurological prognosis, early detection of ASE remains challenging. Postoperative aphasia can result from common neurosurgical conditions, for example, ischemia, direct

injury of the language area, Todd paresis, and NCSE, such as ASE. The combination of neuroimaging modalities and electrophysiological examinations can help to identify the cause. When an unexpected aphasia develops, MRI and EEG should be performed as early as possible. Continuous EEG (cEEG) has a higher diagnostic ability than normal EEG that is conducted for <1 h. If cEEG cannot be implemented, 2 h EEG is an alternative for capturing ictal activity in patients with NCSE.^[4] Simultaneous MRI with diffusion weighting and arterial spin labeling can help in distinguishing between ischemia and seizure.^[15] In addition, regional hyperperfusion in computed tomography perfusion imaging and hypermetabolism in ¹⁸F-fluorodeoxyglucose positron emission tomography are helpful in distinguishing the postictal state from the ictal state.^[1,3,7,8] These modalities allow differentiation of NCSE from Todd paresis, which can last up to 36 h as a postictal symptom.^[13] Furthermore, the etiology can contribute to the prediction of NCSE, because gliomas, metastatic brain tumors, and stroke each tend to induce ASE in neurosurgical diseases.^[1] In practice, it may be difficult to perform all these tests promptly. Therefore, if ASE is suspected, early aggressive intervention should be considered without waiting for all the test results. Further clinical studies are needed to clarify the validity of this treatment strategy.

CONCLUSION

Prolonged ASE can induce verbal and memory impairments. Early intervention with intravenous anesthetics is required to obtain favorable neurological outcomes.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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