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Case Report

Nonconvulsive status epilepticus as sign of tumor recurrence

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ABSTRACT

Status epilepticus (SE) can be a sign of brain tumor progression or recurrence, but there are few reports of nonconvulsive status epilepticus (NCSE) being a sign of tumor progression or recurrence. Moreover, much remains to be elucidated about its clinical course, and outcome. This is the first report of NCSE associated with the progression of a metastatic brain tumor treated by surgical excision of the tumor. The patient was 74-year-old woman. She had a history of craniotomy for tumor resection and gamma knife treatment for multiple metastatic brain tumors originating from breast cancer. She suddenly developed dysarthria and right hemiparesis, followed by convulsive seizures in the right side of her body. Magnetic resonance imaging showed tumor recurrence in the left parietal lobe and worsening edematous changes around the tumor. Antiseizure medication was initiated, however her seizures did not improve; therefore, tumor resection was performed. Postoperatively, her consciousness, seizures, and electroencephalogram findings improved. NCSE caused by brain tumors may be refractory to treatment with antiseizure medications, and early surgical treatment may be useful for seizure control.

1. Introduction

More than 30 % of all brain tumors are associated with epilepsy; epilepsy has been reported to occur in 20–35 % of cases of metastatic brain tumors [1]. Status epilepticus (SE) can be a sign of new brain tumor or metastatic disease [2]; however, there are few reports of nonconvulsive status epilepticus (NCSE) being a sign of tumor progression or recurrence, and much remains to be elucidated about its clinical course, course of treatment, and outcome [3]. The reasons for the limited number of reports include the paucity of clinical data on NCSE associated with brain tumors, and difficulty in distinguishing NCSE from changes in neurological findings due to tumor progression or recurrence [4]. Delays in the diagnosis of and therapeutic intervention for NCSE may contribute to permanent disability and high mortality due to prolonged seizures [5]. Herein, we describe a case of NCSE associated with the recurrence of a metastatic brain tumor, in which early diagnosis and surgical treatment resulted in favorable seizure control, and we present the clinical features and course of NCSE associated with brain tumors. This is the first case report of NCSE associated with progression of a brain tumor successfully treated by surgical excision of the tumor.

2. Case report

The patient was a 74-year-old woman. She had been diagnosed with left breast cancer and received mastectomy and sentinel lymph node biopsy ten years before current presentation. The pathological diagnosis was invasive ductal scirrhous-type carcinoma of the breast. Postoperative hormone therapy was administered. Three years before current presentation, chest CT revealed multiple neoplastic lesions in the right lung. In the same year, video-assisted thoracoscopic lung segmentectomy was performed for the pulmonary neoplastic lesions. The pathology results showed metastatic and primary lung cancer coexisting; however, no adjuvant therapy was performed. Follow-up positron emission tomography/computed tomography-two years before current presentation revealed brain metastasis, and contrast-enhanced magnetic resonance imaging (MRI) was confirmatory (Fig. 1). Tumor lesions were found in the right parietal and occipital lobes, left parietal lobe, and right cerebellum. Mild left paresis and left quadrantanopia were observed. In the same year, craniotomy was performed, and the right parietal and occipital lobe tumor was resected. Pathology results were consistent with a metastatic brain tumor from the primary breast cancer tumor. There were no significant postoperative sequelae. In the same year, gamma knife therapy was performed for three other brain lesions. Subsequently, imaging follow-up was conducted for the metastatic brain tumor, but there was no evidence of recurrence. In the year prior before current presentation, focal clonic seizures involving the right face

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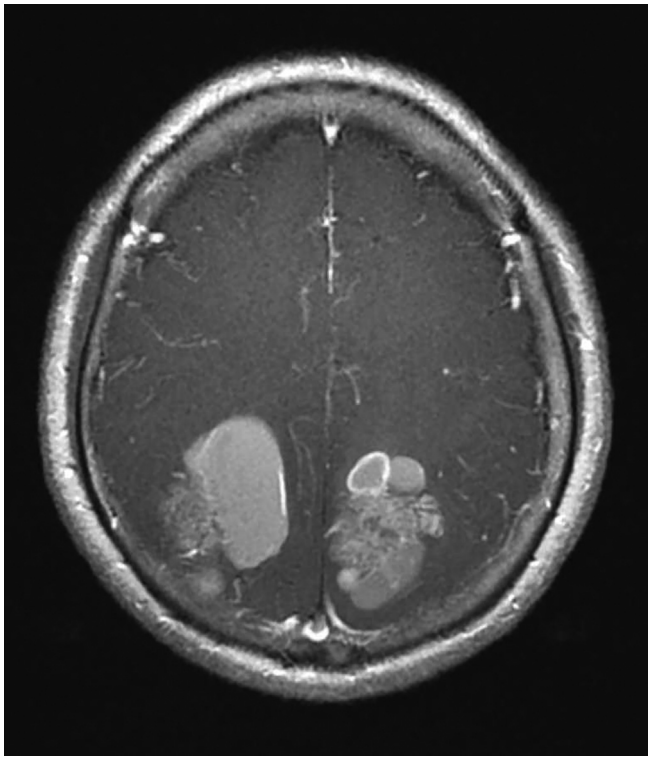

Fig. 1. Contrast-enhanced axial MRI showed a tumor in the bilateral parietal lobe.

and right leg were observed; however, head MRI showed no progression or worsening of the brain tumor. She was treated with valproate sodium and her clonic seizures were controlled. In the present year, she underwent total knee replacement for osteoarthritis of the knee and was transferred to a rehabilitation hospital after the surgery. During rehabilitation, she suddenly developed aphasia and right hemiparesis. MRI showed exacerbation of edematous changes in the left cerebral hemisphere (Fig. 2), including around a known neoplastic lesion in the left parietal lobe, which raised suspicion of metastatic brain tumor progression or a radiation-related tumor, and she was transferred to our hospital for further examination.

When she came to our hospital, her level of consciousness was GCS E3V2M5. She was somnolent and barely able to open eyes when called out; she was unable to communicate; aphasia and right hemiparesis were observed. After arrival at our hospital, a focal clonic seizure was observed involving the right side of her body. It was immediately stopped with administration of diazepam; however, her consciousness did not recover.

In the absence of any infection, electrolyte abnormalities, or other identifiable causes, the patient was considered to have epileptic seizures associated with a brain tumor.

After intravenous fosphenytoin loading bolus administration, she was treated with fosphenytoin at a maintenance dose and levetiracetam (LEV) (1000 mg/day). On the day of admission, video electroencephalogram (EEG) monitoring showed left lateralized periodic discharges with temporal evolution (Fig. 3), and she was diagnosed with NCSE. LEV was increased up to 3000 mg/day.

After increasing the LEV dose, EEG findings showed mild improvement (Fig. 4), but the patient continued to exhibit disturbance of consciousness (GCS E4V2M5), aphasia, and right hemiparesis. Lacosamide (100 mg/day) was added. Regardless of the intensification of medical treatment, there was no change in clinical findings, and occasional focal clonic seizures involving the right face were observed; therefore, craniotomy for left parietal lobe tumor resection was performed 22 days after admission for seizure control. In the surgery, the tumor was dissected and removed completely while using a neuronavigation system and intraoperative neurophysiological monitoring.

Postoperatively, EEG findings improved markedly (Fig. 5), the level of consciousness (GCS E4V3M6) improved, and aphasia and right hemiplegia showed mild improvement. Postoperative contrast MRI demonstrated successful tumor removal (Fig. 6). No convulsive seizures were observed. The pathological findings were consistent with a metastatic breast cancer, and the possibility of a radiation-induced tumor, tumor enlargement, or cerebral edema exacerbation due to cerebral edema as a side effect after radiotherapy were ruled out. The cause of NCSE was considered to be the progression of a metastatic brain tumor. The patient was transferred to a rehabilitation hospital on postoperative day 27 (Fig. 7). After six months, she continued to receive home medical care, and was able to communicate with her family.

3. Discussion

Seizure control is important because epilepsy associated with brain tumors can cause motor and cognitive deficits, and prolonged seizures can lead to permanent disability and a decreased quality

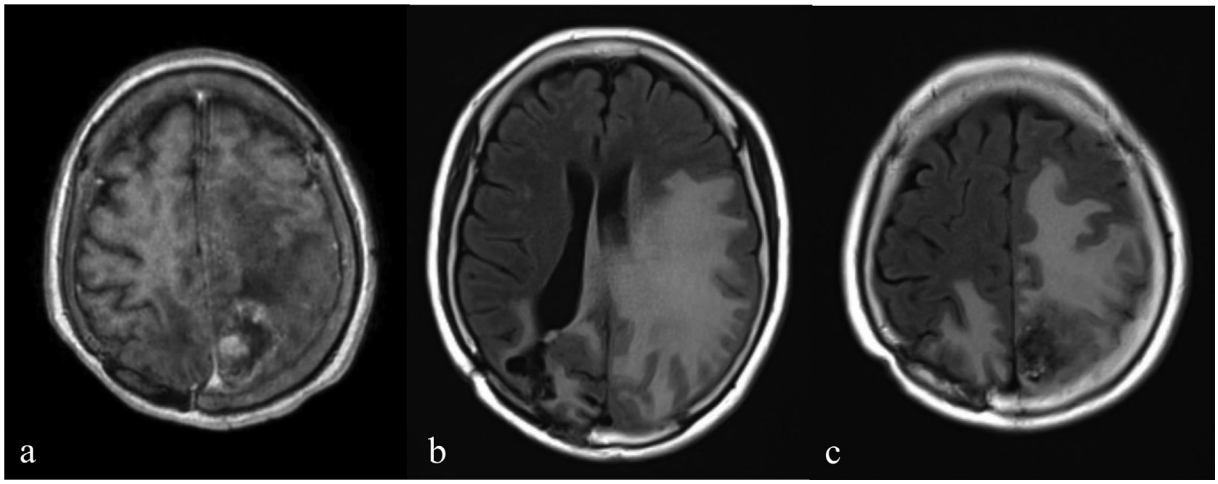

Fig. 2. (a) contrast-enhanced axial showed tumor recurrence in the parietal lobe and (b), (c), fluid-attenuated inversion recovery sequence showed exacerbation of edematous changes in the left cerebral hemisphere.

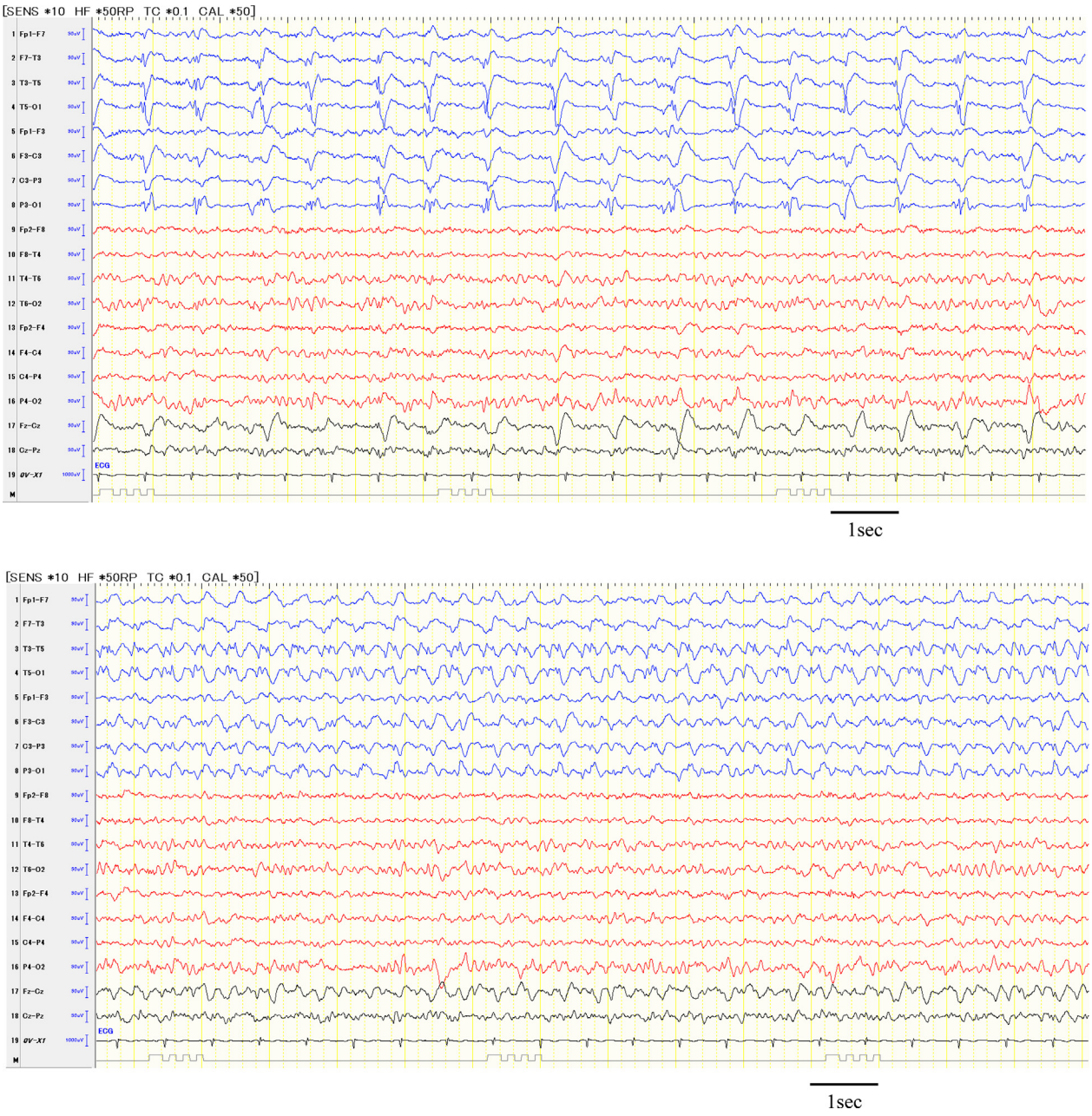

Fig. 3. Preoperative EEG on admission. (a) Left lateralized periodic discharges (LPDs); (b) LPDs with temporal evolution in the left hemisphere.

of life [6,7]. NCSE secondary to trauma, stroke, or a brain tumor is associated with a high mortality rate of 27 % [8], and brain tumor patients with NCSE tend to have an even shorter survival time than brain tumor patients without NCSE [2]. The cause of this high mortality may be the progression of the background disease. It is not clear whether NCSE contributes to subsequent mortality or early diagnosis and whether aggressive therapeutic intervention for NCSE improves the prognosis. However, early diagnosis and seizure control are important in NCSE associated with brain tumors because worsening neurological findings due to NCSE complications may lead to a decreased quality of life, and to shortened survival time as previously reported [2]. As in the present case, by keeping in mind the possibility that NCSE can be a sign of tumor progression, NCSE may be suspected and diagnosed early when brain tumor patients present with findings of unexplained loss of consciousness or seizures, and progression or recurrence is noted on imaging findings. Brain tumor-associated epilepsy is more drug-resistant than other forms of epilepsy, and seizure control can be difficult [1]; furthermore, the administration of high-dose antiseizure medications may be undesirable due to side effects. In the present patient, seizures were difficult to control with medical treatment, and EEG and clinical findings were markedly improved after tumor excision. In cases of NCSE due to secondary causes, treatment of the underlying disease, such as tumor excision, may result in improved EEG and clinical findings, and when NCSE is associated with a brain tumor for which surgery is indicated, surgical treatment should be considered as early treatment for seizures. The suggested reasons why removal of the tumor can control status epilepticus are as follows: Firstly, the presence of brain tumor causes disruption of the blood brain barrier and leakage of various factors such as albumin, glutamate, and tumor necrosis factor [9]. Some of these may result in

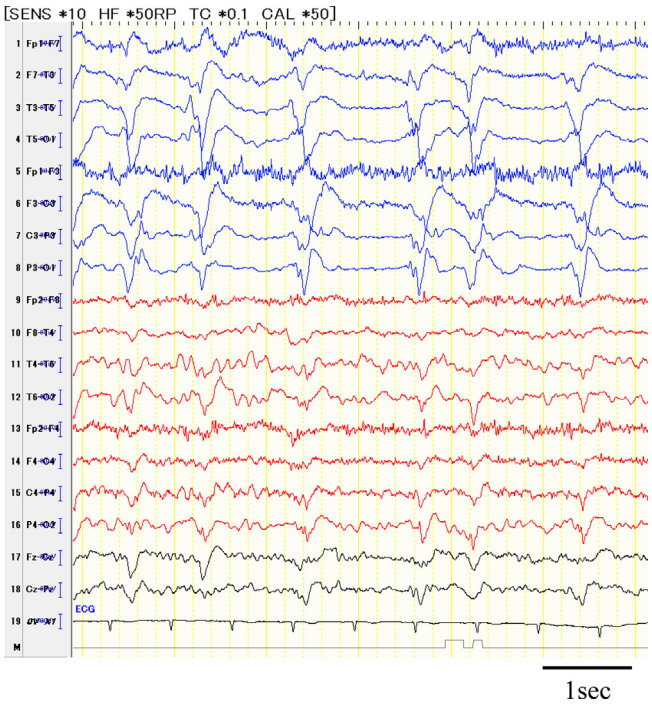

Fig. 4. Preoperative EEG after LEV increased. After increasing LEV dosage from 1000 to 3000 mg, temporal evolution was not observed and ECG findings became stable.

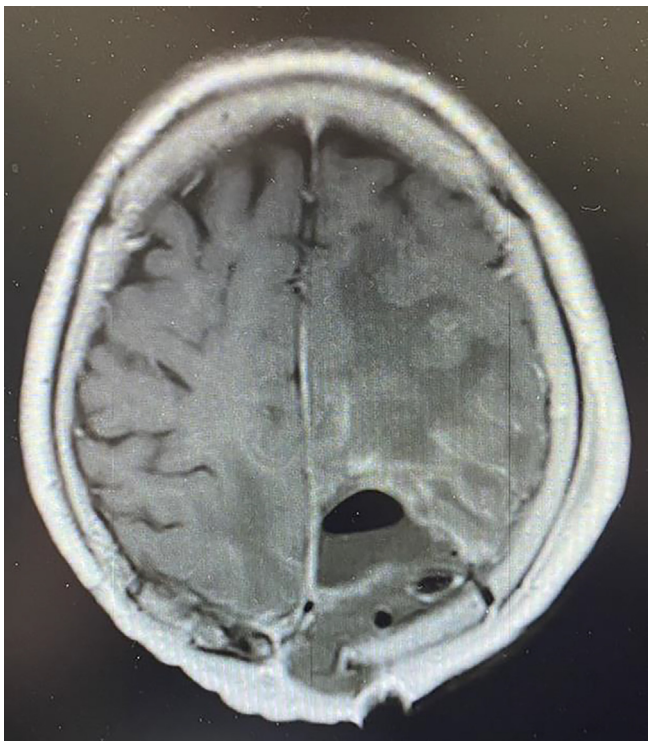

Fig. 6. Postoperative contrast MRI, axial. MRI showed successful tumor removal.

Figure 5 (a)

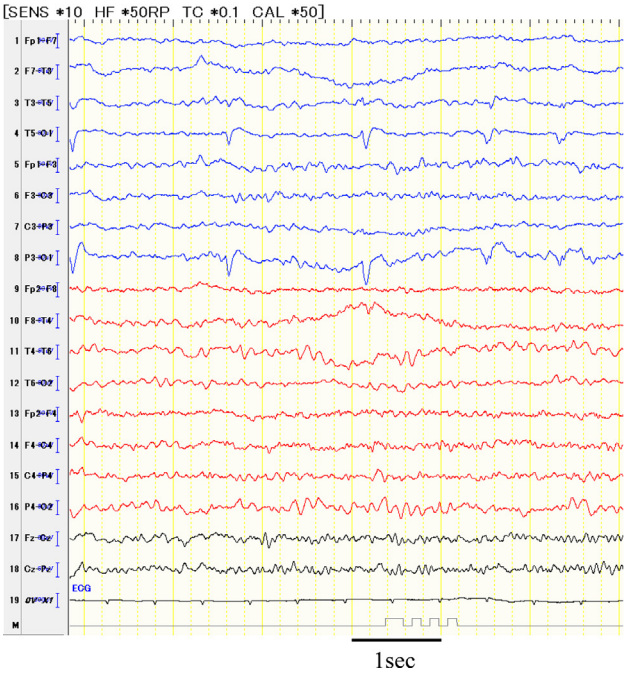

Figure 5 (b)

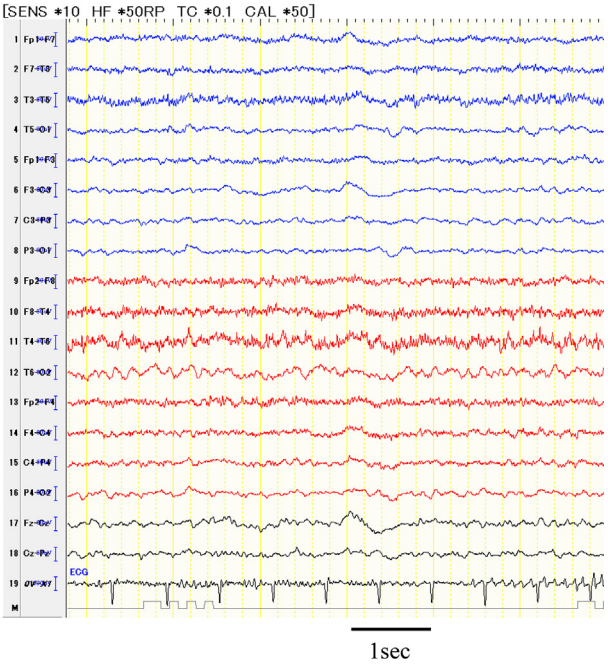

Fig. 5. EEG on postoperative day 8 (a). There are sharply countered periodic discharges on the left. EEG on postoperative day 26 (b). Compared with the preoperative EEG, the postoperative EEG findings were markedly improved.

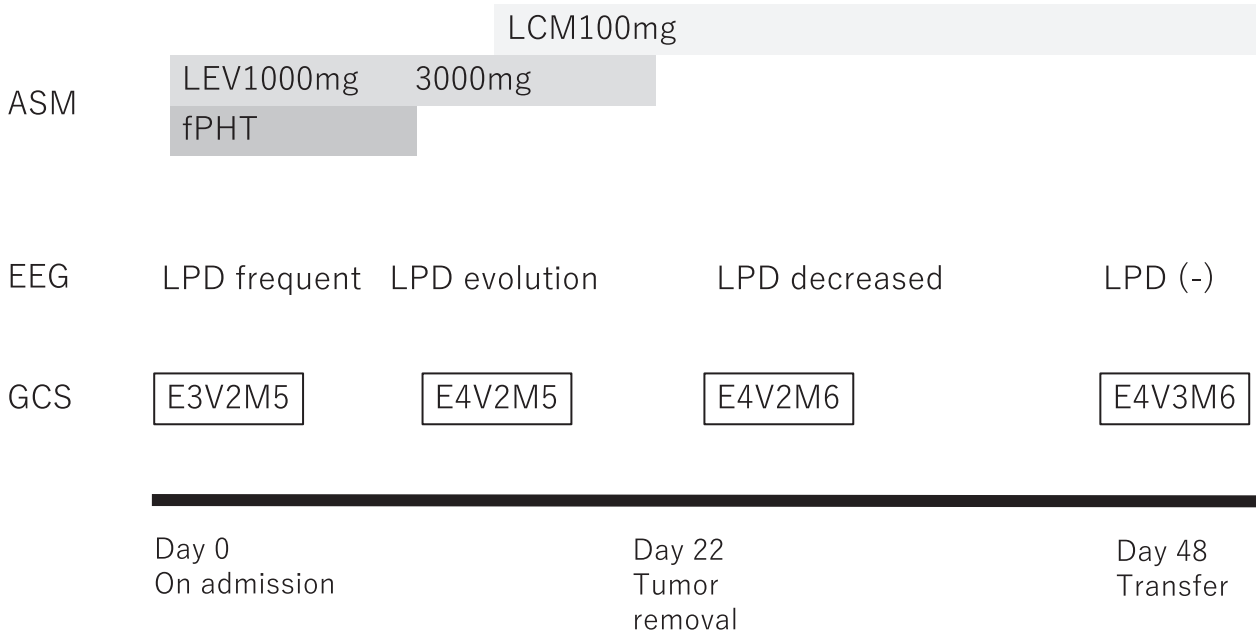

Fig. 7. Time line of patient's clinical course. ASM: antiseizure medication, LCM: lacosamide, LEV: levetiracetam, fPHT: fosphenytoin, EEG: electroencephalography, LPD: lateralized periodic discharges, GCS: Glasgow Coma Scale.

increased neuronal excitability and status epilepticus. Therefore, tumor removal controls the leakage of such factors and leads to seizure control. Secondly, the tumor may cause inflammation of the surrounding tissues, which may also cause seizures [10].

4. Conclusions

NCSE due to a brain tumor may be resistant to treatment with antiseizure medication alone. Early surgical treatment may be useful for the control of NCSE.

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Ethical statement

Written informed consent was obtained from the patient's family for publication of this case report and accompanying images.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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