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Presurgical Evaluation of Epileptogenic Focus in Temporal Lobe Epilepsy by ^{11}C-Flumazenil PET and ^{123}I-Iomazenil SPECT: A Case Report

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Abstract Meticulous neuroradiological evaluations, including ^{123}I-iomazenil (IMZ) single photon emission computed tomography (SPECT) and ^{11}C-flumazenil (FMZ) positron emission tomography (PET), preoperatively disclosed epileptogenic foci in a 16-year-old boy with temporal lobe epilepsy. Interictal scalp electroencephalography showed spikes in the left temporal region. Left hippocampal sclerosis was seen on magnetic resonance imaging. Hypoperfusion in the entire left temporal lobe was seen on ^{99m}Tc ethyl-cysteinate dimer (ECD) SPECT. Hypometabolism over most of the left temporal lobe was apparent on ^{18}F-fluorodeoxyglucose (FDG) PET. An area of hypoperfusion dominating the left temporal lobe was identified on ^{123}I-IMZ SPECT. A low-uptake area in the left temporal lobe was seen on ^{11}C-FMZ PET. Anteromedial temporal lobectomy and multiple subpial transection with intraoperative electrocorticography resulted in satisfactory seizure outcomes. Use of ^{123}I-IMZ SPECT and ^{11}C-FMZ PET appeared to demonstrate the epilepsy focus more localised than ^{99m}Tc ECD SPECT and ^{18}F-FDG PET.

Key words Hippocampal sclerosis; Positron emission tomography (PET); Single photon emission computed tomography (SPECT)

Introduction

For surgery in patients with refractory intractable epilepsy, presurgical diagnosis of the epileptogenic focus has the greatest impact on the surgical outcome. Both magnetic resonance imaging and ictal video encephalographic monitoring are thought to be essential before surgery,[1] although the latter requires the patient to be available until a seizure occurs.[2] Diagnosis of the epileptogenic focus using intracranial electroencephalography (EEG) is thought to be highly accurate, but is quite invasive and requires patient's uncomfortable obligation.[1,3] Many reports have shown that various neuroradiological diagnostic modalities using radioisotopes (RIs) can correctly detect epileptogenic foci, offering a less-invasive alternative to patients. Recently, ^{123}I-iomazenil (IMZ) single photon emission computed tomography (SPECT) has seen practical application[4] and the diagnostic value of ^{11}C-flumazenil (FMZ) positron emission tomography (PET) has also been studied,[5] although few reports concerning these imaging modalities have been published in Japan. We performed ^{123}I-IMZ SPECT and ^{11}C-FMZ PET as well as ^{99m}Tc ethyl-cysteinate dimer (ECD) SPECT and ^{18}F-fluorodeoxyglucose (FDG) PET for presurgical diagnosis in a case of temporal lobe epilepsy. We

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successfully detected the epileptic focus interictally before surgery and present the case herein, along with the clinical course.

Case Report

The case pertains to a 16-year-old boy without any history of febrile seizures or family history of epilepsy. At 3 years old, he suffered complex partial seizures that rendered him immobile and impaired awareness. At 4 years old, these seizures often turned into secondary generalised seizures, which were temporarily controlled by carbamazepine. After reaching 5 years of age, the patient suffered oral automatism followed by extended periods in a twilight state. Magnetic resonance imaging (MRI) at that time did not reveal any abnormalities. Clonazepam and zonisamide were added, but seizures remained uncontrolled. From 12 years old, the patient often engaged in quarrels resulting from his memory disorder. Gabapentine and topiramate were concomitantly administered, but proved completely ineffective. A sense of fear and depersonalisation, in addition to abdominal discomfort, appeared from 14 years of age. EEG showed interictal spikes in the left temporal region (Figure 1). We had two complex partial seizures (CPSs) with postictal nose wiping during overnight video tape recorder (VTR)-EEG recordings, both of which originated from his left sphenoidal and anterior temporal leads. VTR showed that he touched his nose by his left hand after seizures. MRI demonstrated left hippocampal sclerosis (Figure 2a). Left temporal lobe epilepsy associated with hippocampal sclerosis was diagnosed. No functional MRI studies were performed.

WISC-III examinations performed two years before surgery showed the score below the general average, VIQ 71, PIQ 60 and TIQ 62, respectively. Among them he was especially poor at vocabulary and verbal expression. He successfully graduated from his junior high school.

Hypoperfusion throughout the entire left temporal lobe was seen on ^{99m}Tc ECD SPECT (Figure 2b), although ^{123}I-IMZ SPECT disclosed hypoperfusion restricted to the medial portion of the left temporal lobe (Figure 2c). Hypometabolism was observed in a broad area across the entire left temporal lobe on ^{18}F-FDG PET (Figure 2d). The hypometabolic area was seen to predominantly involve the inner side of the left temporal lobe on ^{11}C-FMZ PET (Figure 2e). According to a presurgical RI study, ^{123}I-IMZ SPECT and ^{11}C-FMZ PET showed more focal accumulations than ^{99m}Tc ECD SPECT and ^{18}F-FDG PET.

Based on these findings, the seizure focus was determined to be located in the vicinity of the head of the hippocampus on the inner side of the left temporal region. Electrocorticography (ECoG)-guided epilepsy surgery was performed without invasive monitoring using intracranial electrodes. Intraoperative ECoG showed spikes not only on the inner side of the temporal lobe, but also in the temporal pole, posterior cortex, amygdaloid body, and head of the hippocampus. In addition to medial temporal lobectomy, multiple subpial transection (MST) was performed on the lateral surface of the temporal lobe. Although he has occasional simple partial seizures and rare CPS after surgery, his family is quite satisfied with this outcome. His status is categorised as Engel class IIB/ILAE class 3.

Discussion

Clarifying the focus of localisation-related seizures prior to epilepsy surgery is essential. However, reaching a proper diagnosis of the focus based solely on the state of the seizures is often difficult.[6] For accurate diagnosis, EEG is inevitable, but interictal single EEG offers a detection rate of only 55.5% even with activators such as hyperpnoea, photic stimulation, and sleep.[7] Digital EEG with video monitoring is thus often recorded for a long period using

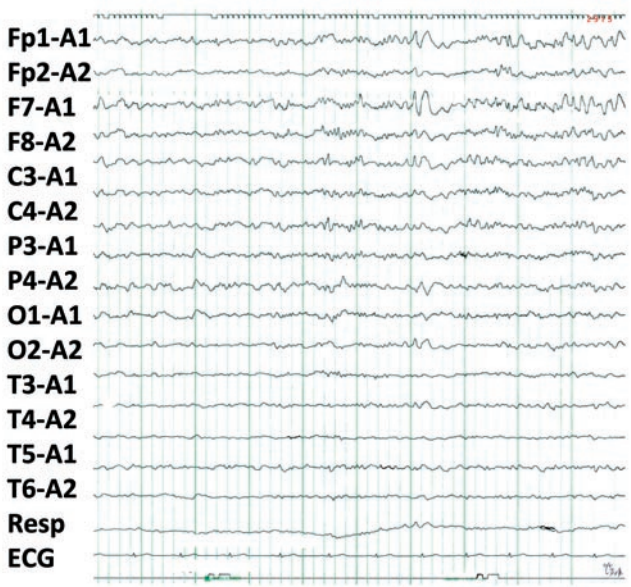

Figure 1 Interictal electroencephalography at 14 years old. Spikes are apparent in the left temporal region.

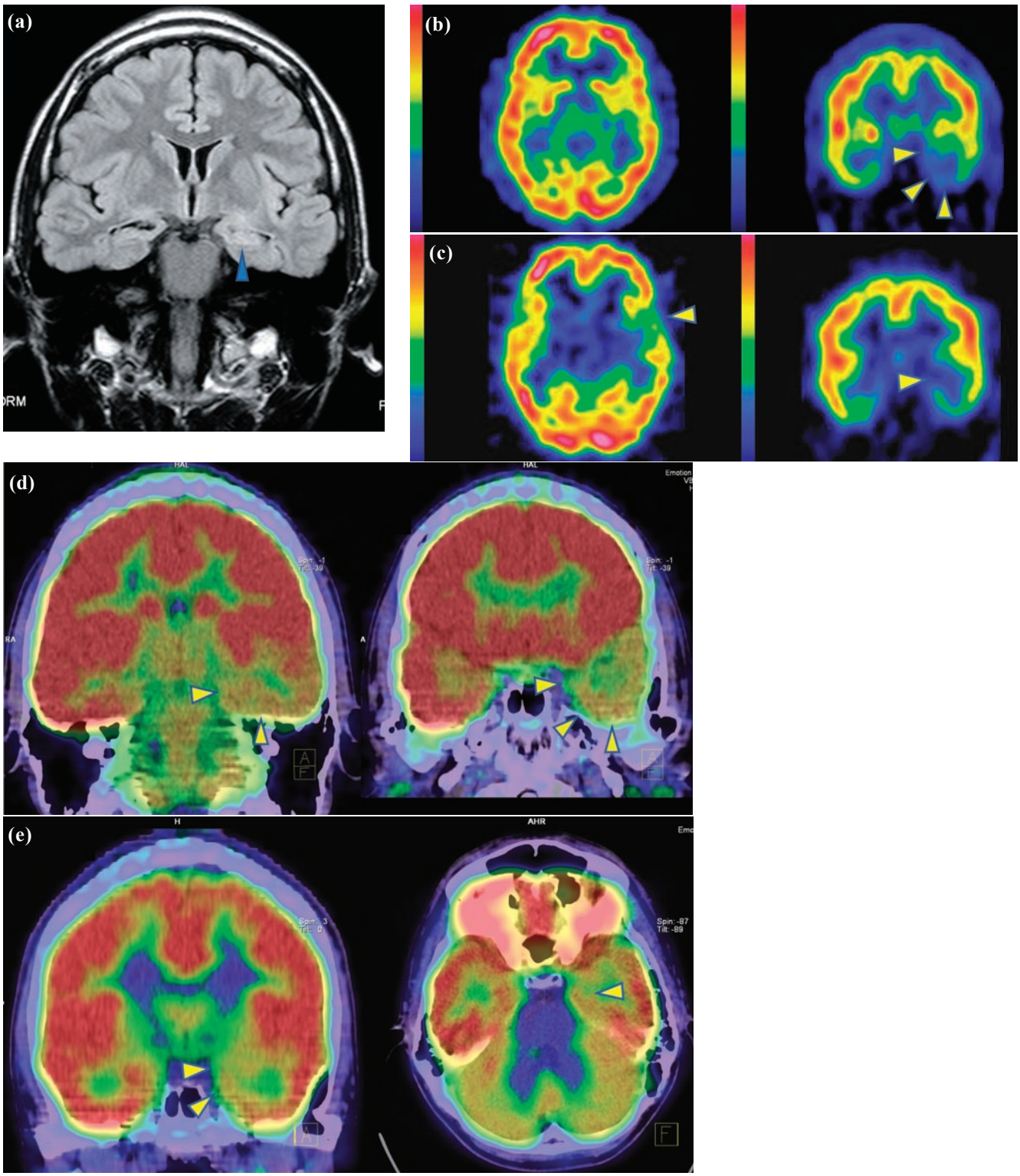

Figure 2 (a) Brain fluid-attenuated inversion recovery (spin echo: echo time, 105.0 msec; repetition time, 9000 msec) magnetic resonance imaging of the brain at 14 years old, showing left hippocampal sclerosis. (b) An area of hypoperfusion is observed over the entire left temporal lobe on ^{99m}Tc ethyl-cysteinate dimer single photon emission computed tomography (SPECT). (c) The area of hypoperfusion dominates the inner side of the left temporal lobe on ^{123}I-iomazenil SPECT. (d) A hypometabolic area is seen over a broad area across the entire left temporal lobe on ^{18}F-fluorodeoxyglucose positron emission tomography (PET). (e) The hypometabolic area dominates the inner side of the left temporal lobe on ^{11}C-flumazenil PET.

intracranial electrodes,[1-3] although this is quite an invasive procedure for patients. In recent years, ^{123}I-IMZ SPECT has been introduced to visualise benzodiazepine receptors and is now approved and applied clinically in Japan. The usefulness of this method has been reported.[4] Moreover, PET with ^{11}C-FMZ, a central benzodiazepine receptor antagonist, has shown diagnostic usefulness.[5]

Although interictal EEG recordings showed left anterotemporal abnormal discharges and coronal MRI (FLAIR) suggested higher intensity in his left medial temporal region, his left hippocampus seemed relatively smaller. It did not exclude the possibility of the right pathology. It may require invasive EEG recordings, which was not suitable for him. We, including his family, wanted to skip invasive modalities and performed these investigations. The examinations performed in this study, using four different RI substances, all suggested abnormalities in the left temporal region. Among these modalities, the results with IMZ and FMZ nicely matched the MRI findings of left hippocampal sclerosis and the epileptic focus detected intraoperatively. Use of ^{123}I-IMZ SPECT and ^{11}C-FMZ PET appeared to demonstrate the epilepsy focus more localised than ^{99m}Tc ECD SPECT and ^{18}F-FDG PET.

Anterior temporal lobectomy remains one of the standard surgical methods for mesial temporal lobe epilepsy. As intraoperative ECoG showed residual spikes on the lateral surface of the temporal lobe, multiple subpial transection (MST) was added on the superior and middle temporal gyri. The importance of intraoperative ECoG has been described in many reports,[8] and in this case suggested a remaining focus. Outcomes for this patient have proven satisfactory to date, although only 1 year has passed since surgery.

In the present case, no intellectual deterioration was observed and the patient was able to enter high school with mental stabilisation after surgery. Taking into consideration the relatively poor quality of life for this patient, with frequent intractable complex partial seizures since childhood, surgery may have been indicated at an earlier age. MRI at 5 years old probably appeared normal due to the limited resolution available at the time. However, MRI performed 9 years later clearly showed left hippocampal sclerosis. According to Wiebe et al, seizures were controlled in 8 of 40 cases in which drug treatment was administered, but for the other 32 cases in which epilepsy surgery was performed, seizures disappeared in 58% within 1 year.[9]

Koepp et al reported that for intractable temporal lobe epilepsy with normal MRI findings, ^{11}C-FMZ PET clearly visualizes the seizure foci.[10] Identifying the epileptic focus using ^{11}C-FMZ PET and/or ^{123}I-IMZ SPECT proactively is important even in the absence of abnormalities on MRI. Epilepsy surgery should always be kept in mind for patients with intractable temporal lobe epilepsy.

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