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Insulinoma Presenting as Medically Intractable Temporal Lobe Epilepsy

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We describe a female insulinoma patient who presented with recurrent attacks of abnormal behavior, confusion, and seizure. Her interictal EEG showed epileptiform discharges on the left temporal area, therefore she was initially misdiagnosed as temporal lobe epilepsy. In the video-EEG monitoring, hypoglycemic state was detected during the seizure attack, so the right diagnosis was made after the endocrinologic investigations. After surgical removal of the tumor, the patient became seizure-free, and no abnormality was found in the follow-up EEG after six months. Since insulinoma shares some common clinical and EEG features with complex partial seizure of temporal lobe origin, insulioma should be included in the differential diagnosis for medically intractable temporal lobe epilepsy. **(2014;4:21-23)**

Key words: Insulinoma, Hypoglycemia, EEG, Temporal lobe epilepsy

Introduction

Epilepsy is a relatively common neurological disease and the diagnosis is largely based on clinical presentation. Various conditions can mimic the symptoms of epileptic seizures such as psychogenic non-epileptic seizures, hypoglycemia, paroxysmal kinesmogenic dyskinesia, and hemiballism. Differential diagnosis of epilepsy also includes psychiatric illness, cardiac arrhythmia, autonomic dysfunction, and metabolic abnormalities.

Insulinoma is a rare neuroendocrine tumor derived mainly from pancreatic islet cells. It occurs in 1 to 5 per million patients per year. It is more common in women and in patients over 50 years old.[1] Insulinoma usually secretes insulin in short bursts causing fluctuation of blood glucose level according to the blood insulin level, so patients can show intermittent hypoglycemic symptoms, such as altered consciousness, abnormal behavior, psychiatric symptoms and even seizure.[2] In particular, the clinical features in insulinoma patients are similar with those in complex partial seizures originated from the temporal lobe. With these clinical characteristics, approximately 20% of insulinoma patients are initially misdiagnosed. Medically intractable epilepsy is one of the commonly encountered misdiagnosis in insulinoma patients. With the low incidence of insulinoma and the paroxysmal occurrence of insulinoma-induced hypoglycemic symptoms, the diagnosis of insulinoma is often delayed.[3-5]

We report a patient presenting with recurrent episodes of abnormal behavior, subsequently diagnosed as medically intractable temporal lobe epilepsy. The patient was confirmed later to have physiologic non-epileptic seizures due to an insulinoma, which were completely controlled following surgical resection.

Case

A 50-year-old woman with unremarkable family history was referred to our epilepsy clinic for recurrent episodes of abnormal behaviors lasting for 6 months. Her family described that she showed stereotyped behaviors and blank expression for the first time. The patient did not respond for up to 20 minutes, and then recovered spontaneously. The attacks were often followed by convulsions with involuntary micturition and accompanied with prolonged period of drowsiness and confused state continuing for up to one hour. The episodes occurred every 3 weeks in the first two months. Later the frequency of attacks gradually increased up to once a week.

The physical and neurological examinations were all normal. Laboratory examinations including fasting blood glucose and glycated hemoglobin (HbA1C) showed no abnormality. While epilepsy-dedicated brain MRI showed no abnormal findings, interictal EEG revealed occasional spikes on the left temporal area (Fig. 1). Under the diagnosis of left temporal epilepsy, oxcarbazepine 300 mg/day was introduced. However, her seizure was not controlled even after higher dosage of oxcarbazepine nor co-treatment with other antie-

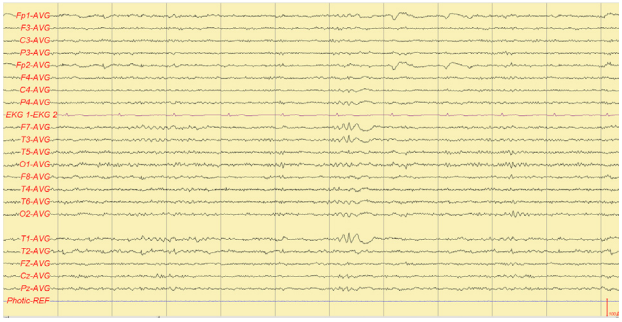

Figure 1. interictal EEG shows spike and wave complex on the left temporal area.

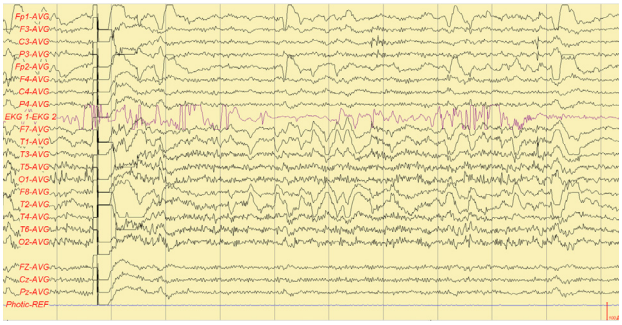

Figure 2. During the video-EEG monitoring, only diffuse slow activity is observed during the seizure attack.

pileptic drugs such as lamotrigine, valoproic acid, levetiracetam, pregabalin and topiramate. During the medical treatment, the longest period for symptom free that she experienced was only two weeks. Four months later, the attacks occurred almost every day. The patient was hospitalized to perform video-EEG monitoring for the further characterization of the attacks and the possible presurgical evaluation. Habitual convulsion was observed at 3 AM, but the EEG showed only diffuse slow activity during the attack (Fig. 2). However, a finger stick glucose level during the attack was only 36 mg/dL. On further questioning, it was apparent that her previous symptoms tended to occur in the early morning or several hours after meals, and that the post-attack confusion could be shortened if she drinks glucose-containing beverages. The subsequent endocrine evaluation suggested insulinoma, and contrast-enhanced Abdominal CT scan revealed an enhanced mass in the head of the pancreas (Fig. 3). After surgical removal of the tumor, the blood glucose level turned to normal. A benign insulinoma was also confirmed by histopathological evaluation. No abnormality was found in the follow-up EEG after six months, and the patient remained seizure-free without medication during the two year follow-up.

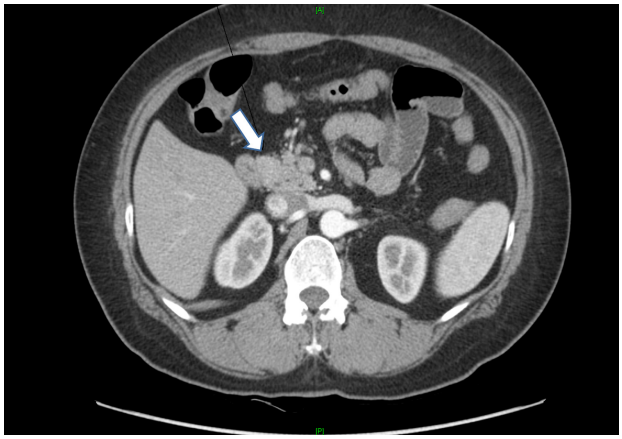

Figure 3. Abdominal CT shows enhancing mass lesion in the pancreas head (arrow).

Discussion

We reported a patient of insulinoma seen in the epilepsy clinic as adult onset medically intractable epilepsy. In this patient, the manifestations of recurrent confusion, abnormal behavior, episodes of altered consciousness and seizure combined with the epileptiform discharge on the left temporal lobe on EEG were highly indicative of temporal lobe epilepsy. Therefore, the patient received high dose antiepileptic drug for a long time due to the misdiagnosis. The patient could be correctly diagnosed after the exacerbation of the symptoms via video-EEG monitoring. As in our patient, there is usually a long interval from presentation to diagnosis range from 1 month to up to 30 years.[6] The delayed diagnosis is caused by several factors. Aside from the rare incidence of insulinoma, the symptoms of insulinoma frequently lack specificity, including nonspecific confusion, personality change, bizarre behavior, amnesia, seizure, and even incidental dystonia (Tan 2002). The manifestations of insulinoma share many features with common neurological and psychiatric disorders. In addition, fasting blood glucose level can be normal in some patients because of the pulsatile nature of insulin secretion. Finally, hypoglycemia itself is able to induce the counter-regulatory hormonal responses such as glucagon.[7]

EEG is commonly used for the differential diagnosis of epileptic seizure and non-epileptic seizures. However, EEG can be misleading in insulinoma patients since hypoglycemia can affect EEG, causing diffuse or focal slow activity. Moreover, epileptiform discharges induced by hypoglycemia are also found in diabetic patients.[8] Our patient was previously healthy and the MRI scan revealed no abnormality, so it can be inferred that the presence of epileptiform

discharges on EEG was caused by hypoglycemia as a result of hyperinsulinemia. This phenomenon was previously observed in patients with insulinoma, and they could be either interictal epileptiform discharge or even the electrical seizures.[3,4] Hypoglycemia can also activate focal abnormality in the EEG in epilepsy patients who have an old lesion in the cortex.[9] Experimental studies confirmed that severe hypoglycemia was able to induce spontaneous synchronic discharges, thus even generate a hypermetabolic state and further deplete the brain energy reserve.[10] This seizure-like event cannot be controlled by the common antiepileptic drugs. Interestingly, hypoglycemia seizure induced in animal tends to be originated in the mesial temporal structures, such as amygdala and hippocampus, which have a low threshold for seizure.[11] Taken together, these findings are helpful to explain the phenomenon that hypoglycemic seizure in insulinoma is medically intractable and can present as complex partial seizure with temporal origin.

In summary, our patient shows that seizure caused by insulinoma-induced hypoglycemia with epileptiform discharge on the interictal EEG. Although insulinoma is a benign and curable situation, it may be fatal if unrecognized. Our report reiterates the importance of evaluating the metabolic cause of seizure disorders. Because insulinoma shares some common clinical and EEG characteristics with complex partial seizure of temporal lobe origin, insulioma should be included in differential diagnosis for medically intractable temporal lobe epilepsy.

Acknowledgments

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