Reversible Magnetic Resonance Imaging Abnormality in A Case of Diabetic Hyperglycemia related Epilepsia Partialis Continua

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Abstract

Seizure can be the first symptom of diabetic hyperglycemia and cause transient abnormalities in neuroimaging studies. Herein, we report the case of a 72-year-old woman with a one-month history of intermittent clonic movement of the left upper limb and neck. Laboratory testing revealed non-ketotic hyperglycemia. Electroencephalography showed asymmetrical background with delta activity over right frontal-temporal lobe. Brain magnetic resonance imaging revealed leptomeningeal and cortical enhancement in the right parieto-occipital area with T2 hypointensity in the corresponding subcortical area, a finding which has been rarely reported. She was treated successfully with oral hypoglycemic agents and short-term use of valproic acid. Follow-up brain magnetic resonance imaging three months later showed total recovery of the signal changes with residual mild cortical atrophy in the same region. For patients with diabetic hyperglycemia and prolonged seizures which results in abnormalities of brain imaging consistent with leptomeningeal and cortical enhancement, valproic acid may be beneficial in abolishing the seizures. (J Intern Med Taiwan 2011; 22: 438-443)

Keywords: Diabetic hyperglycemia, Epilepsia partialis continua, Magnetic resonance imaging, Valproic acid

Introduction

Diabetic hyperglycemia (DH) has been documented to induce seizures[1,2], and may cause transient signal changes on magnetic resonance imaging (MRI) following seizures[3,4,5]. Transient subcortical hypointensity on T2 and fluid-attenuated inversion recovery (FLAIR) images have been identified to be related to non-ketotic hyperglycemia[4,5]; however, leptomeningeal and cortical enhancement were rarely seen. We herein report a case of DH with epilepsia partialis continua (EPC), showing reversible MRI abnormalities of focal leptomeningeal and cortical enhancement with overlying subcortical hypointensity, which was associated with the epileptic focus on

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electroencephalography (EEG). She had complete resolution of symptoms after one-week of treatment with oral hypoglycemic agents and valproic acid.

Case report

A 72-year-old female presented to our hospital with a one-month history of intermittent clonic convulsions of the left upper extremity accompanied with head tilting toward the left side. Initially, each episode lasted for approximately one minute, stopped spontaneously, and occurred one to two times per day. She was totally alert during and following the attacks. However, the symptoms progressed as the frequency of attacks increased to 30 times per day, and caused her embarrassment in social situations. She denied any medical diseases in the past and did not take any medications. She had no history of fever or infectious diseases prior to this event, and denied history of head injury, seizure, or stroke.

Upon physical examination, the patient was alert and oriented. She had a body temperature of 36.5°C, regular pulse rate of 58 beats per minute, blood pressure of 146/75 mmHg, and normal heart sounds. Cranial nerve examinations, muscle strength of four limbs, and the deep tendon reflexes were normal. Her neck was supple without meningeal signs, and physical examinations of other systems were unremarkable. The patient was observed to have frequent clonic convulsions of the left upper extremity accompanied with the head turning toward the left side during the daytime and sleep. There was neither post-ictal confusion nor Todd's paralysis.

Laboratory testing showed: serum glucose, 280 mg/dL; serum osmolarity, 292 mOsmol/L; HbA1c, 13.3%; sodium, 134 mEq/L; potassium, 3.3 mEq/L; serum chloride, 101 mEq/L; and BUN, 21 mg/dL. No ketoacidosis was found in the urine or serum. A series of examinations revealed no evidence of diabetes-related microvascular or macrovascular complications. EEG showed asymmetrical background with delta activity over right frontal-temporal lobe (Fig. 1). Brain computed tomography (CT) and non-enhanced T1 weight MRI (Fig. 2A) showed unremarkable findings while contrast-enhanced T1-weighted MRI disclosed focal leptomeningeal and cortical enhancement in the right parieto-occipital lobe (Fig. 2B). T2-weighted (Fig. 2C) and fluid-attenuated inversion recovery (FLAIR) (Fig. 2D) MRI showed cortical swelling

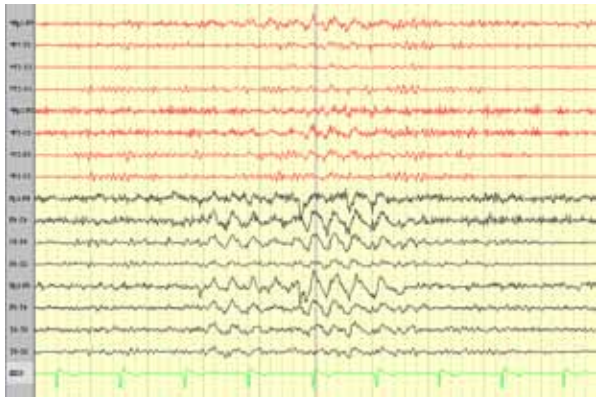

Fig 1. Awake EEG demonstrated asymmetrical background with delta activity over right frontal-temporal lobe.

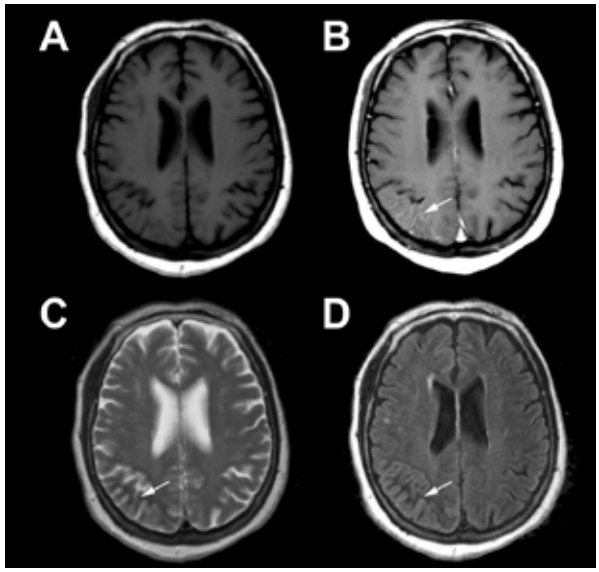

Fig 2. Axial MR T1-weighted images show no signal abnormality (A). Contrast-enhanced T1-weighted images depict contrast enhancement of the leptomeninges and overlying cortex in the right parieto-occipital lobe (arrow) (B). Linear subcortical hypointensities (arrows) are present on the T2-weighted (C) and FLAIR images (D).

with linear subcortical hypointensities in this region. The diffusion weighted image (DWI) and apparent diffusion coefficient (ADC) map showed no significantly signal abnormality in the corresponding area. Lumbar puncture was done on suspicion of meningoencephalitis. A normal opening pressure of 120 mmH_2O was detected, and cerebrospinal fluid analysis disclosed normal cell count and biochemistry results, and no evidence of bacterial and viral infections. Serological and autoimmune studies were unremarkable.

The patient was treated with oral hypoglycemic agents (metformin 500 tid and glimepiride 2 mg qd) after admission. The frequency of seizure activity decreased to 10 times per day while her glucose level was around 100-200 mg/dL. Three days later, valproic acid with the dose of 400 mg q8h was prescribed because of an insufficient seizure control. The seizures stopped completely in two days, and the valproic acid was gradually tapered over a period of two weeks. In the subsequent follow-up, no further seizures were noted. Her blood glucose was well controlled (HbA1c 5.8%) and there were no hypoglycemic episodes. The follow-up brain MRI three months later showed complete disappearance of the signal abnormalities, but mild cortical atrophy of the corresponding cortex was found (Fig. 3).

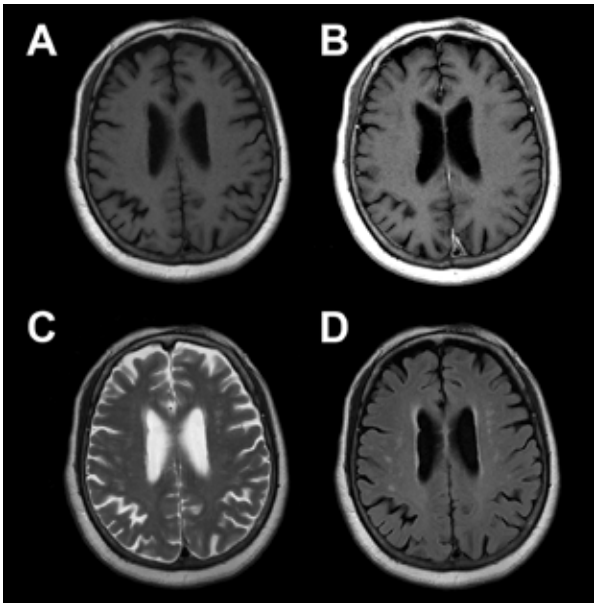

Fig 3. Follow-up MRI 3 months after treatment showing mild cortical atrophy (A), and no focal contrast enhancement of the corresponding area (B). Total resolution of the subcortical hypointensity on T2-weighted (C) and FLAIR images (D) are noted.

Discussion

Epileptic seizures in patients with DH are not uncommon in clinical practice, and may be the initial presentation of diabetes mellitus. In previous reports, patients were noted to have a moderately high blood glucose with a mean value ranging from 318 to 532.9 mg/dL, mildly elevated serum osmolarity, and a lack of ketoacidosis[2,6]. The most common seizure types were focal motor seizures and epilepsia partialis continua, which commonly involved the upper limbs[6,7] from the epileptic focus at fronto-parietal motor cortex. It is unknown why our patient has a seizure activity and MR abnormalities localizing at right parieto-occipital lobe. We supposed that the patient might have a previous slight ischemic insult in this region, which could lower the seizure threshold in a state of hyperglycemia. The correlation between epileptic focus and hyperglycemic status is still unclear. A previous report said that occipital lobe seizure may be correlated to high HbA1c.[8]

In addition to seizures, focal neurological symptoms such as movement disorders may be the first presentation of non-ketotic hyperglycemia. It has been well documented that hyperglycemia can induce hemichorea–hemiballisum, especially in Asian, elderly patients with a predominance towards females. Lesions are usually located at the contralateral subthalamic nucleus and pallidosubthalamic pathways. Most of these patients present a hyperintense signal change on T1-weighted MRI on contralateral basal ganglia[9].

The pathophysiological mechanism of seizures associated with hyperglycemia is not completely understood. It has been shown that

hyperglycemia has a pro-convulsant effect that can lower the seizure threshold[1,2,6]. Hyperglycemia also causes an osmolality gradient between the intra- and extracellular neuronal environment that can lead to intracellular dehydration and induce seizures. Moreover, non-ketotic hyperglycemia increases GABA metabolism, resulting in neuronal hyperexcitability[10]. Although the glucose level in our patient was relatively lower compared to other case, her high HbA1c level indicated a persistently elevated glucose over the previous months, thereby explaining why she might have seizures.

Leptomeningeal enhancement in patients with hyperglycemia-related seizures has rarely been reported. In our patient, subcortical T2 hypointensities in addition to leptomeningeal and cortical enhancements in the epileptic area were observed. Although these findings are very rare, we believe that prolonged seizure activity would give rise to these MRI abnormalities. Enhancement of the leptomeninges following seizures is supposed to occur due to seizure-induced dilatation of leptomeningeal vasculatures. Cortical enhancement is believed to be the result of seizure-induced hypoxia and acidosis with subsequent alteration of vascular permeability and breakdown of the blood-brain barrier, leading to contrast extravasation[3,10]. Central nervous system infection and malignancy may have the similar MRI abnormalities; however, these diagnoses were excluded in our patient based on her clinical features and CSF analysis. Furthermore, the reversible abnormalities of MRI and EEG studies supported that the patient had a transient seizure disorder. Prolonged seizures may actually induce neuronal injury with subtle cortical gliosis and atrophy[3,4], which was also observed in our patient.

The mean duration of seizure control in patients with DH is about 36 hours, and the longest time of seizure control is 11 days[6]. In general, antiepileptic drugs (AED) are not necessary for hyperglycemia related seizures because seizures are typically resolved after blood glucose is normalized[6,7,11]. Adequate hydration and aggressive blood glucose control, either with insulin or oral hypoglycemic agents, are crucial. However, hypoglycemia should be prevented because it can also cause seizures. In refractory cases of epilepsia partialis continua, prolonged seizures can result in neuronal damage, which further lead to worsening of seizure activity. Previous reports suggest that phenobarbital may be used in these patients with diabetic hyperglycemia who develop status epilepticus[11]. Phenytoin, the popular used AED, can precipitate hyperglycemia, and worsen the seizure disorder[12]. We found that short-term use of valproic acid, a GABAergic AED, was effective for seizure control in our patient, which is in agreement with previous reports that GABA is depleted in DH, causing neural hyperexcitability.

Conclusions

In addition to T2 subcortical hypointensity, leptomeningeal and cortical enhancement of MR abnormalities may be found in patients with DH-related prolonged seizure. In cases of DH with insufficient seizure control after a strict blood glucose control, the use of valproic acid, a GABAergic antiepileptic drug, may be effective.

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糖尿病高血糖合併局部持續性癲癇造成可逆性腦部核磁共振影像變化 - 病例報告

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摘　要

糖尿病合併癲癇症在臨床並不少見，但大部分病人出現癲癇併發症的時間很短，影像學上多無特異發現，臨床上也不需使用抗癲癇藥物治療。我們報告一位72歲新診斷的糖尿病患者，以局部持續性癲癇發作來表現，且時間已長達一個月。腦部核磁共振影像出現罕見且獨特之異常變化。住院後病人血糖雖然控制良好，但仍持續有癲癇發作現象。於是開始給予抗癲癇藥物治療，使用數天後癲癇即有效獲得控制。後續追蹤之核磁共振影像顯示原本異常之訊號已完全恢復正常。我們建議爾後如有糖尿病患者合併類似之核磁共振影像異常時，除了積極控制血糖外，提早且短期的使用抗癲癇藥物也許有助於更快速地控制此類患者之癲癇症狀。